EVALUATION OF UPPER GASTROINTESTINAL ENDOSCOPY IN DYSPEPSIA WITH SPECIAL REFERENCE TO HELICOBACTER PYLORI IN NON ULCER DYSPEPSIA

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MADURAI MEDICAL COLLEGE, MADURAI.

CERTIFICATE

This is to certify that this dissertation titled "**EVALUATION OF UPPER GASTROINTESTINAL ENDOSCOPY IN DYSPEPSIA WITH SPECIAL REFERENCE TO HELICOBACTER PYLORI IN NON ULCER DYSPEPSIA**" submitted by **DR. NITHYA.S**. to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by her under our direct supervision and guidance

DR. M. MUTHIAH, M.D.
Professor of Medicine,
Chief, VI Medical Unit,
Department of Medicine,
Madurai Medical College,
Madurai.

DR.A.AYYAPPAN, M.D.
Professor and Head
Department of Medicine,
Madurai Medical College,
Madurai

DECLARATION

I**, Dr.Nithya.S,** solemnly declare that the dissertation titled "**Evaluation of upper gastrointestinal endoscopy in dyspepsia with special reference to Helicobacter pylori in non ulcer dyspepsia"** has been prepared by me.

This is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the rules and regulations for the award of MD degree (branch I) General Medicine.

Place: Madurai

Date: **Dr.Nithya.S.**

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CONTENTS

ABBREVIATIONS

DU – Duodenal Ulcer

GERD – Gastro Esophageal Reflux Disease

GI – Gastrointestinal

HP – Helicobacter pylori

H.pylori – Helicobacter pylori

IBS – Irritable Bowel Syndrome

LSES – Lower Socioeconomic Status

MALT – Mucosa Associated Lymphoid Tissue

MSES – Middle Socioeconomic Status

NSAID – Non Steroidal Anti Inflammatory Drugs

NUD – Non Ulcer Dyspepsia

OGD – Oesophago Gastro Duodenonoscopy

PPI – Proton Pump Inhibitors

PCR – Polymerase Chain Reaction

RUT – Rapid Urease Test

Th – T Helper

INTRODUCTION

Upper gastrointestinal endoscopy is routinely performed everyday for a number of patients in the department of Medical Gastroenterology, Government Rajaji Hospital. It is generally considered the diagnostic method of choice in uninvestigated dyspepsia because it allows identification of structural causes of dyspepsia and most importantly excludes carcinoma, but examination of all patients is hard to perform. The reason is the high annual incidence of dyspepsia. The issue is even more important in developing countries like ours with limited access to diagnostic services. There is no generally accepted consensus about the age cut off for upper GI endoscopy, because it mainly depends on the regional age-specific incidence of gastric cancer.

The association of Helicobacter pylori with various gastrointestinal disorders has been studied in the past few years. The relation between peptic ulcer and H.pylori is well established throughout world literature. The ultra rapid urease test has been used in the past few years to study the presence of organism in the endoscopic specimen. Though there are several methods used to detect the organism, most of them are expensive and cumbersome to perform. This test provides a quicker and cheaper means to study the organism with a high degree of sensitivity and specificity.

The association of H.pylori with peptic ulcer and gastric adenocarcinoma was suggested by its discoverer Barry Marshall. In 1984, it was again described shortly after subsequent studies assessed its role in GERD and non ulcer dyspepsia. It was found to be one of the etiological factors for gastric adenocarcinoma and gastric MALTomas in 1991. It was identified as a grade I carcinogen in 1994 and the importance of its eradication in patients with a positive family history of carcinoma was stressed. Its association with non ulcer dyspepsia is less well understood despite several studies in the past. The histology of non ulcer dyspepsia has also not been studied in detail in the past. The few studies which are available indicate that there could be a role for H.pylori but has not been determined with accuracy.

REVIEW OF LITERATURE

DYSPEPSIA

Dyspepsia refers to chronic or recurrent pain or discomfort centered in the upper abdomen. The term dyspepsia originates from the Greek words dys and pepsin which means poor and digestion respectively.[1, 2] It has been used rather loosely including symptoms of vague upper abdominal or periumbilical discomfort or pain, early satiety, abdominal bloating, nausea with or without vomiting and belching. The possibility of serious organic disease should be considered when alarm symptoms or signs are present which include the following -

1. Age older than 55 years with new-onset dyspepsia
2. Family history of upper gastrointestinal cancer
3. Unintended weight loss
4. Gastrointestinal bleeding
5. Progressive dysphagia
6. Odynophagia
7. Unexplained iron-deficiency anemia
8. Persistent vomiting
9. Palpable mass or lymphadenopathy
10. Jaundice[3]

Diseases presenting with dyspepsia fall into two general categories: organic and functional. Overall, most patients with dyspepsia have no underlying identifiable disease process. The commonest organic causes of dyspepsia are peptic ulcer disease, gastroesophageal reflux, biliary tract disease, and gastric cancer.[2] Dyspeptic symptoms may be present in both organic and functional gastrointestinal disorders. Certain symptoms and physical signs as mentioned before may help to differentiate these organic causes from functional dyspepsia.

The ROME III criteria for functional dyspepsia are as follows -

One or more of:

Bothersome post prandial fullness

Early satiety

Epigastric pain

Epigastric burning

AND

No evidence of structural disease (even after performing endoscopy) that is likely to explain the symptoms.

The above criteria must be fulfilled for the past three months with symptom onset at least six months before diagnosis. [1,4]

Based on the different symptom complex present in the majority of the non ulcer dyspepsia sufferers the patients are classified into the following groups after confirming the diagnosis by endoscopy for easier means of selection of medical therapy-

1. Ulcer-like: predominant symptom is pain centered on the upper abdomen

2. Dysmotility-like: predominant symptom is an unpleasant or troublesome nonpainful sensation or discomfort centered in the upper abdomen and may be characterized by or associated with upper abdominal fullness, early satiety, bloating or nausea.

3. Reflux-like dyspepsia,

4. Essential (non-specific) subgroups. These were proposed by the International working party in 1988.[1,5,6]

The presence of retrosternal burning pain or heartburn reliably indicates GERD as per various studies and dysphagia almost always indicates organic esophageal pathology.

TABLE 1 DIFFERENTIAL DIAGNOSIS OF DYSPEPSIA[1]

Peptic ulcer disease	7-25%
GERD	2-29%
Gastric or esophageal cancer	1-3%
Biliary disease	<5%
Pancreatic disorders	<5%
Metabolic disorders	<5%
Celiac disease	Rare
Functional dyspepsia	50-60%

Functional dyspepsia may represent up to 60% of all patients with dyspeptic symptoms. In the majority of patients with a negative conventional evaluation, specialized studies such as esophageal pH monitoring, esophageal manometry, lactose tolerance testing, antroduodenal motility study and radioscintigraphy may identify an underlying organic cause for the symptoms but are not routinely indicated for all patients as initial evaluation techniques. Various studies have been done in the past to determine the cut off age above which endoscopy should be performed as the initial diagnostic technique. No specific age has been determined to date. Missing early (and hence curable) gastric cancer is often of greatest concern to the clinician

contemplating empirical therapy, especially in an older patient. Fear of gastric cancer has to be taken into account when planning the management of dyspepsia. It is generally accepted that the incidence of serious lesions like gastric malignancy is low below the age of 50 years and endoscopy may not be essential in these patients without alarm symptoms. The yield from endoscopy in patients being investigated for dyspepsia increases with advancing age but is generally low.

A potential benefit of endoscopy is that gastric ulcers can be confirmed to be benign by performing biopsy.[7] Endoscopy permits gastric biopsy specimens to be taken to diagnose H. pylori status; rapid urease testing is relatively inexpensive and is sensitive (95%) and specific (up to 100%). However, a single biopsy may miss 5–10% of cases, and recent antibiotic use or antisecretory therapy will increase the false-negative rate. Moreover, there is limited and unconvincing evidence that endoscopy leads to improvement in the patient's satisfaction scores in dyspepsia. Cost effectiveness is the other consideration. Amongst the various causes of dyspepsia, functional dyspepsia rates highest and it may not be cost effective to choose endoscopy as the first investigation. Various studies have proved a good correlation between alarm symptoms and the presence of serious

organic disease and thus a good symptom analysis can be used to pick up organic disease at an earlier date.[8, 9]

Review of past literature reveals that endoscopy may not be needed in younger patients without alarm symptoms.[10]

Gillen et al found in their study that upper GI malignancy is extremely rare in patients <55 years presenting with uncomplicated dyspepsia and, when found, is usually incurable. Consequently, concern about missing underlying curable malignancy is not a valid indication for endoscopying patients <55 years presenting with uncomplicated dyspepsia. [11]

Marmo et al concluded that the age threshold for endoscopy should be lowered in males to decrease the risk of missing cancers, and can be safely increased in females without affecting outcomes. In patients with uncomplicated dyspepsia, the combination of age and gender provides a better discriminant power than age alone. [12]

Williams et al have found in their study that young patients with simple dyspepsia are over investigated. A majority can be treated safely with antacids and/or histamine receptor type 2 antagonists. [13]

Christie et al concluded that gastric cancer is rare below the age of 55 (7.8% of all cases) and, even in the presence of established open access endoscopy, presents with suspicious symptoms or signs in 96% of cases.

The age limit for screening uncomplicated dyspepsia can be raised safely to 55 years. [14]

HELICOBACTER PYLORI

After its discovery by Warren and Marshall in the year 1982 and its association with gastritis, it has been extensively studied in the pathogenesis of various gastric lesions. It is a spiral gram negative bacterium which is motile and mainly colonizes the zone beneath the gastric mucus which overlies the gastric epithelial cells. The organism may be found in any part of the stomach but prefers the antrum where there parietal cells are scanty in number or absent. H.pylori can be demonstrated in saliva, gastric juice and dental plaques by the sensitive PCR technique. Oro oral and feco-oral are likely pathways of transmission.

The infection is more prevalent in the developing countries (up to 90%) and is facilitated by conditions of overcrowding, poor living facilities. Low socioeconomic status and low education level are also known to increase infection rates.[1,2] Rate of acquisition of infection increase with age and there is no specific gender predilection. There are high infection rates among smokers.[15]

PATHOGENESIS OF GASTRIC LESIONS

Cag A gene possessing strains are common in people with peptic ulcer or adenocarcinoma. All HP strains possess Vac A gene but only 40% are toxigenic. The characteristic motility of the organism allows it to move rapidly through viscous mucus. Once the organism is safely encased in the mucus, it is able to fight the gastric acidity with the help of urease and converts urea (of which there is abundance from saliva and gastric juices) into ammonia, which is a strong base, thus creating a cloud of acid neutralizing chemicals around the organism and protecting it from gastric acidity. [1, 2, 16, 17, 18]

Another defense that the organism has is that the body's natural defenses cannot reach the bacterium in the mucus lining of the stomach. The immune system responds strongly to the infection with a host of immune cells which unfortunately cannot get through the gastric lining. But they are localized just outside the stomach lining and thus a vicious cytotoxic immune response ensues, producing gastritis and peptic ulceration. It may not be the organism itself which causes peptic ulcer but in fact the host response to H.pylori.

Although the organism is non invasive, the bacterium stimulates chronic gastritis by provoking a local imflammatory response in the

underlying epithelium due to a variety of cytotoxins. Once infection in the antrum is established, there is depletion of antral somatostatin and stimulation of gastrin release from G cells. Subsequent hypergastrinemia stimulates acid production by the parietal cells, leading to duodenal ulceration. The role of HP in gastric ulcer is less clear but HP probably reduces gastric mucosal resistance to attack from acid and pepsin .[1]

Host response to infection is characterized by an acute neutrophilic infiltrate in the acute stage followed by a chronic inflammatory cell infiltrate in the later stages, the Th1 response predominating.

The following types of chronic gastritis have been found to be associated with HP infection -

Type A: atrophic in nature and have parietal cell antibodies

Type B: no parietal cell antibodies

Type AB: atrophic and patchy

Chronic gastritis in HP has been found to be associated with intestinal metaplasia and increases risk of gastric adenocarcinoma. HP infection has been very strongly linked to duodenal ulcer, the prevalence rates reaching close to 100%. Eradication of HP in DU gives awarding results. The most serious lesion caused by HP is gastric cancer. The pathogenesis is represented as follows by Correa's multi step hypothesis.[19]

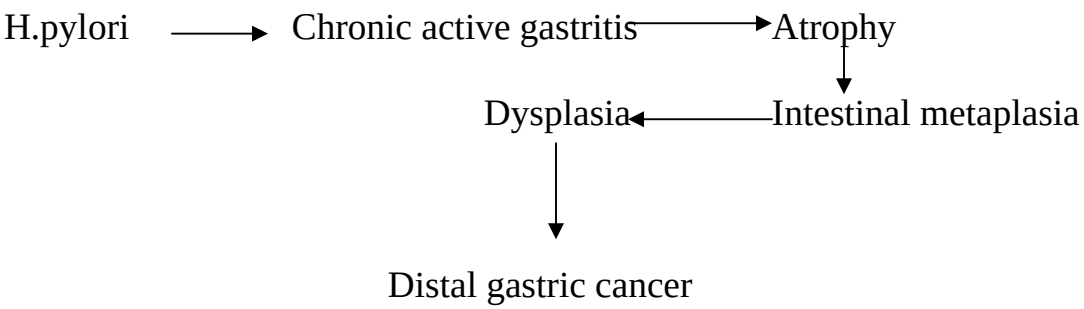

TABLE 2 Association of HP with various gastric disorders[1]

Chronic gastritis	50-65%
Duodenal ulcer	95-98%
Gastric ulcer	60-75%
Non ulcer dyspepsia	50-60%
Gastric adenocarcinoma	six fold increase
Gastric MALToma	93-98%

DIAGNOSIS OF INFECTION

The presence of H.pylori in the stomach can be detected by several invasive and non invasive methods.

Invasive	Non invasive
Culture Histology of biopsied specimen Rapid urease test	Serology Urea breath test Stool antigen test, PCR, urine antigen

The choice of the test used depends upon the accuracy, cost, availability and whether the patient will be undergoing endoscopy.[2, 3, 20] Stool antigen tests are increasingly being used as simple non invasive methods for H.pylori diagnosis. Serology is useful as a screening test but cannot differentiate between current and past infection.

TABLE 3 COMPARISONS OF VARIOUS METHODS OF DETECTION OF HP [21]

Feature	**Histo**	**Culture**	**RUT**	**ELISA**	**UBT**	**SAT**	**PCR**
Sensitivity (%)	**90**	**86**	**88-92**	**90-100**	**95-100**	**91**	**93-96**
Specificity (%)	**88**	**100**	**92-100**	**91-100**	**95-100**	**93**	**100**
Invasive	+	+	+	-	-	-	-
Expensive	+	+	-	-	-	-	+
Results within 24 hrs	-	-	+	-	+	+	+
Can confirm eradication	-	-	-	-	+	-	+
Accuracy affected by recent treatment with PPI/antibiotics	+	+	+	-	+	-	-
Histo-histology, +=yes, -=no, PCR=polymerase chain reaction, RUT=rapid urease test, UBT= urea breath test, SAT= stool antigen test, ELISA= enzyme linked immunosorbent assay							

MANAGEMENT OF DYSPEPSIA AND H.PYLORI INFECTION

The clinician evaluating a patient with dyspeptic symptoms should recognize the limitations of history taking and physical examination in this setting. The principal utility of the clinical history and physical examination is to-

(1) Identify patients with GERD and NSAID-induced dyspepsia

(2) Identify patients with alarm symptoms who may require early investigation.

Patients who have typical symptoms of reflux disease should be managed as having GERD. Patients whose symptoms are predominantly related to bowel function may have IBS and should be treated appropriately. Alarm features are used to try and identify patients who need early investigation with endoscopy. The negative predictive value was always >97% in various trials, reflecting the fact that upper gastrointestinal malignancy was a rare diagnosis.

There are 5 initial approaches to the management of dyspepsia:

(1) Empirical acid suppression;

(2) A non-invasive test for H pylori, with a urea breath test, stool antigen test, or serology, and reserving endoscopy for positive cases;

(3) A noninvasive test for H pylori and eradication therapy for positive cases;

(4) Empirical H pylori eradication therapy without testing;

(5) Early endoscopy.[3]

PATIENTS WITH DYSPEPSIA AND ALARM SYMPTOMS

Due to the small but clear-cut increase in the risk of upper gastrointestinal malignancy, new-onset alarm symptoms or new onset of symptoms after the age of 55 years should prompt early endoscopy. This cutoff was chosen because the risk of malignancy in most populations is <10 per 100,000 below the age of 55 years. The probability of detecting an early gastric cancer is therefore very low below this age.[3]

PATIENTS WITH DYSPEPSIA AND NO ALARM SYMPTOMS

The optimal management strategy for the patient who presents with new-onset dyspepsia and no alarm features has been dominated by testing for H pylori and treating all positive cases empirically with antibacterial therapy. However, there are other choices, including no testing but empirical medical therapy (e.g., an antisecretory agent) with any subsequent investigation reserved for failures or immediate evaluation by upper endoscopy in all cases and targeting therapy based on the results.[3]

In primary care, empirical antisecretory therapy remains popular. Only a minority of patients with dyspepsia has peptic ulcers, and even fewer have cancer. Therefore, in 1985, the American College of Physicians recommended, based on a literature review of outcomes and cost, that antisecretory medical therapy is preferable for patients without obvious organic disease who are younger than 45 years of age. The American College of Physicians further suggested that endoscopy (rather than a barium series) should be reserved for patients who have little or no response to therapy after 7–10 days or for patients whose symptoms have not resolved after 6–8 weeks. However, whether this age threshold is still applicable and the utility of empirical therapy now continue to be debated, especially in terms of continuing such treatment on a long-term basis in those with undiagnosed H pylori infection.

The 3 strategies that have undergone intense evaluation are empirical acid suppression, H pylori test and treat, and early endoscopy. Preliminary data suggest that H pylori test and treat is more cost-effective than empirical PPI therapy in patients with dyspepsia. As a strategy, the efficacy of H pylori test and treat will vary according to whether the test is performed in primary or secondary care and the prevalence of infection in the population.

"Cure" is to be offered to the patients who are infected and an alternate approach for those who test negative.

THE MANAGEMENT OF DOCUMENTED NON ULCER/FUNCTIONAL DYSPEPSIA

1. Initial PPI therapy
2. Acid suppression,
3. Prokinetic therapy,
4. H pylori eradication therapy, and
5. Psychological therapies.[22]

Overall, the only therapies that have established efficacy in functional dyspepsia are H pylori eradication and PPI therapy. H pylori eradication is the most cost-effective approach in patients who are positive because this treatment is only given once for a long-term effect. In H pylori–negative patients with functional dyspepsia and those who fail to respond to eradication therapy, a one month course of PPI therapy may be warranted.

The association between H.pylori and the non ulcer dyspepsia has been analyzed for many years and various studies have tried to prove the association so that these patients can be subjected to eradication therapy. But definite evidence is lacking. A study performed in Germany by Bajorsky et al concluded that HP-infection per se contributes to dyspepsia. 85% HP-

positive dyspeptic patients improved after HP-eradication, when other potential organic causes for dyspepsia had been ruled out. However, many patients did not completely recover but the symptoms only partly decreased which parallels the persistence of part of the inflammatory infiltration in the gastric mucosa. This emphasizes the importance of HP-gastritis as an organic disease causing dyspeptic symptoms.[23]

The first national workshop on H.pylori was held in Mumbai in the year 1997 and the significant conclusions were as follows-

1. The prevalence of H.pylori infection in healthy or asymptomatic persons in India varied from 31-84 %.

2. Prevalence mainly depends on the age, socioeconomic status, housing, sanitation and methods used for diagnosis.

3. Age related prevalence studies show that in India, infection occurs at an earlier age than in the west.

4. The frequency of H.pylori in non ulcer dyspepsia varies from 60-85% and no correlation was found between the degree of gastric inflammation and symptoms of non ulcer dyspepsia.

5. There is no large study on the histological picture of the gastric mucosa and its correlation to symptom response.

6. Invasive techniques have been the preferred mode of diagnosis of H.pylori in India; of these tests rapid urease test has been most popular, both the commercially available kits and the in house developed ones.

Anitha Kamath et al compared the sensitivity and specificity of a commercially available urease test and an in house prepared urease test using histology as the gold standard. The in house urease test was cheap and more sensitive than the commercially available helicochek kit. [24]

Thayumanavan L et al, Madurai studied the prevalence of H.pylori in gastroduodenal diseases during routine upper gastrointestinal endoscopies at Madurai and concluded that the organism is widely prevalent in southern parts of Tamil Nadu, the rapid urease test is cheap, simple and useful for detecting the organism, and the prevalence of infection was nearly as high in non ulcer dyspeptics (66%) as those with DU (86%).[25]

In the research setting, culture should be included in the protocol for confirming eradication, till the urea breath test is widely available. Serology is ideal for epidemiological studies.[26]

Warren Marshall observation proved that greater than 90% of DU patients were infected compared to 40% of controls. [27]

Four endoscopic surveys showed H.pylori infection in 43-79% of NUD patients. These numbers were well above control in three of these

surveys. At least 50% of infected persons had no symptoms. Some have found that infected patients are likely to have reflux like or ulcer like symptoms. [28, 29]

The EUROGAST study group showed a positive correlation between the prevalence of gastric cancer and H.pylori in different parts of the world. The correlation was convincing and statistically significant. [30]

PC Jain et al studied the presence of H.pylori in patients with upper gastrointestinal symptoms using the rapid urease test and found significant prevalence of the organism in both ulcer and non ulcer dyspepsia. [31]

There have been very few studies on the histopathological aspects of non ulcer dyspepsia and its relation to H.pylori. One study done in Nigeria found that significant mucosal lesions were found in patients who were infected with H.pylori despite normal endoscopy.[32] Studies from India are lacking.

ERADICATION OF HELICOBACTER PYLORI

All patients suffering from gastric or duodenal ulcers who are infected with H.pylori should be treated with antimicrobials regardless of whether they are suffering from the initial presentation of the disease or from recurrence. Drugs known to cause dyspepsia should be discontinued wherever possible. However, the issue of eradicating H.pylori in non ulcer

dyspepsia remains controversial. Recent studies suggest that H.pylori should be eradicated even in non ulcer dyspepsia. [1, 47, 48] H.pylori eradication is defined as negative test for H.pylori at least 28 days after therapy.

FACTORS WHICH MODIFY TREATMENT

1. Bismuth and PPIs specifically inhibit the bacterial enzyme urease so that urease based tests might fail to detect residual infection or recurrence.

2. H.pylori tends to move to the proximal stomach during suppression of acid secretion. So biopsy based tests become inaccurate

3. C^{13} and C^{14} urea breath tests are most accurate because they sample the whole stomach and so regarded as gold standard to confirm eradication.

4. Serology is not useful to confirm eradication as it takes at least 6 months for the antibody titer to fall significantly

5. Dual therapy with a two week combination of omeprazole or ranitidine bismuth citrate and either amoxicillin or clarithromycin eradicated H.pylori in 50-80%. In triple therapy, eradication may be around 50-70%. One week, twice daily PPI based triple therapy eradicates in about 90%. Second line regimens include seven days treatment with omeprazole and thrice daily amoxicillin and metronidazole or a PPI based regimen.

TABLE 4 TRIPLE REGIMENS WITH AMOXICILLIN AND METRONIDAZOLE

	REGIMEN 1	REGIMEN 2	REGIMEN 3
Drug	Omeprazole+ amoxicillin+ metronidazole	Ranitidine+ amoxicillin+ metronidazole	Bismuth+tetracycline/ amoxicillin+ metronidazole
Dose (daily)	40mg once+ 500mg thrice+ 400mg thrice	300mg once+ 750mg thrice+ 500mg thrice	120mg 4 times+ 500mg 4 times+ 200-400mg 4 times
Duration	7 days	12 days	2 weeks
Efficacy	95%	90%	60-90%
Side effects	Diarrhea, nausea		

These standard triple regimens have been replaced by shorter regimens which contain amoxicillin or clarithromycin along with a proton pump inhibitor. These regimens are equally effective in eradicating the organism.

TABLE 5 LOW DOSE TRIPLE THERAPY[2]

	REGIMEN 1	REGIMEN 2
Drugs	PPI+ Clarithromycin+ Metronidazole	PPI + Amoxicillin+ Clarithromycin
Dose(daily)	Once/twice daily+ 250mg twice+ 400mg twice	Twice + 1 gm twice+ 250-500 mg twice
Duration	7 days	
Efficacy	90%	90%
Side effects	Uncommon: diarrhea, nausea with metronidazole	

QUADRUPLE THERAPY

PPI (once/twice daily), colloid bismuth sub citrate(120mg four times daily), tetracycline(500 mg four times daily), metronidazole(400-500mg 3-4 times daily)

Duration of therapy: seven days

Efficacy: 85-95%

Side effects: diarrhea, nausea[2]

SEQUENTIAL THERAPY

Day 1-5

Proton pump inhibitors twice a day

Amoxicillin one gram twice a day

Day 6-10

Proton pump inhibitors twice a day

Clarithromycin 500 mg twice a day

Tinidazole 500 mg twice a day.

Sequential therapy gives an eradication rate of around 98%. The sequential therapy gave a higher eradication rate than the conventional triple therapy and it has been suggested that it should be made the standard eradication therapy for H.pylori.[33]

AIMS AND OBJECTIVES

The aims of the study were as follows-

1. To study the value of upper gastrointestinal endoscopy in patients with new onset previously uninvestigated dyspepsia with and without alarm symptoms
2. To study the prevalence of H. pylori in non ulcer dyspepsia in various age groups
3. To study the histopathological aspects of non ulcer dyspepsia.

MATERIALS AND METHODS

THE STUDY GROUP

The study was conducted on inpatients or outpatients visiting the Gastroenterology department and medical wards. Approval from the ethical committee was obtained. The study was a cross sectional study conducted for a period of one year between June 2007-08.

Inclusion criteria

1. Patients aged >18 years

2. New onset previously uninvestigated dyspeptic symptoms for more than three months' duration including-

1. Upper abdominal pain/discomfort

2. Early satiety/Post prandial fullness

3. Abdominal bloating

4. Recurrent belching

Exclusion criteria

1. Intake of antibiotics, metronidazole, PPI or NSAIDs at present or within past 15 days

2. Acute gastrointestinal bleeding

3. Pregnancy

4. Severe systemic illness

5. Symptoms suggestive of reflux disease

6. Gallstone disease.

7. Patients refusing endoscopy.

METHODS

A total number of 282 patients were studied out of which 224 were included in the study as per the inclusion and exclusion criteria. They were also classified according to the socioeconomic status using the Modified Kuppuswamy classification[34] which utilizes three parameters namely education, occupation and monthly income. Socioeconomic status score was assigned to each patient. Informed consent was obtained from all patients before the start of the study.

A detailed history was elicited from the patient about the type and duration of dyspepsia. The presence or absence of alarm symptoms was also noted as previously mentioned. Baseline investigations were done to rule out major systemic illness. An ultrasonographic examination of the abdomen was done to rule out gallstone or mass lesion. Patients with documented gall stone disease were excluded from the study.

A detailed informed consent was obtained from the patients for undergoing upper GI endoscopy. All patients were advised overnight fasting and OGD was performed on empty stomach in the morning. OGD was

performed with a flexible fibreoptic endoscope and the mucosa of the stomach and pylorus was analyzed for any lesions. Biopsies were taken from the fundus, body and antral mucosa for histopathology. An additional sample was taken from the antral mucosa for the tissue ultra rapid urease reaction. After sterilization, the scope and biopsy forceps were washed with sterile distilled water so that no error in the test occurred due to changes in pH.

THE ULTRA RAPID UREASE TEST

This test is a modification of the standard urease test so that a positive result is available almost immediately. The basic principle behind the test is that H.pylori produces large quantities of urease which rapidly hydrolyses urea to ammonia. The urea in the test solution is hydrolyzed to ammonia by the preformed urease present in the H.pylori positive antral biopsy specimen. The color of the solution changes from yellow to pink due to the change in pH of the solution. The test solution consists of 0.5ml of freshly prepared 1% urea (W/V) in sterile distilled water to which is added two drops of 1% phenol red as a pH indicator in clean capped bottles.

PROCEDURE AND RESULTS

A single antral mucosal biopsy was taken within five centimeters of the pylorus and the specimen was placed immediately within the test

solution and remained undisturbed. H.pylori positive specimens changed the color of the solution from yellow to pink and the results were read within one minute. Negative test specimens were observed for 12 hours stored in a refrigerator. Though the intensity and velocity of color change varied with patients, those who tested positive developed a faint pink color change around the biopsy specimen immediately. The whole solution changed to pink color immediately in some whereas in others a faint pink color developed over a period of time. Bacterial load is said to be the factor affecting velocity and intensity of color change. Solutions without H.pylori remained yellow throughout.

MERITS AND DEMERITS

Various studies have compared the diagnostic accuracy of the RUT with all other diagnostic modalities. The test has been shown to have a sensitivity and specificity of 90% and 100% respectively. The test does not give false positive results unlike the conventional urease test in which contaminants like Proteus and Pseudomonas may give a positive result with prolonged incubation. The rapidity of the test is said to be due to the urea in water solution which is unbuffered like the Christenson's urea broth. The test solution is very inexpensive and easy to prepare. The endoscopist

detects the infection even before the instrument is withdrawn. Treatment can be instituted at once and the outpatient reviews can be reduced.

The main disadvantage is that the procedure is invasive requiring endoscopy and biopsy. Though mostly colonization of bacteria in the gastric mucosa is concentrated at the antrum, the distribution may be patchy and biopsy from multiple sites is said to further increase the sensitivity of the test. This procedure cannot be used for screening a general population where a serum based test like ELISA is more practical.

Biopsy specimens from the body, fundus and antrum were analyzed for histopathological changes after staining with routine hematoxylin and eosin.

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2002).** Using this software, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS AND ANALYSIS OF OBSERVED DATA

EPIDEMIOLOGY

Majority of the patients were from in and around Madurai. The age of the patients ranged from 18 to 82 years. Patients were nearly equally distributed in all age groups. Out of 224 patients included in the study, 21 (9.3%) were from the lower socioeconomic class, 85 (37.9%) from the upper lower class, 91 (40.6%) from lower middle class and 27 (12%) from the upper middle class. The lower and upper lower classes were combined together as lower socioeconomic status (47.4%) and the lower middle and upper middle classes were combined together as middle socioeconomic status (52.6%).

The mean age of the study population was 44.7$\pm$14.6 years. The age distribution of patients is shown in table 8.

TABLE 6: AGE DISTRIBUTION OF PATIENTS

Age group(in years)	18-29	30-39	40-49	50-59	>60
MSES	19	30	21	16	20
LSES	19	26	22	23	28
TOTAL	38	56	43	39	48
%	17	25	19.6	17	21.4
Mean			44.7 years		
Standard deviation			14. 6 years		

Among the 224 patients, 135 were male patients (60.3%) and 89 were female (39.7%). Out of the 135 male patients, 29 were chronic smokers (21%).

SYMPTOMATOLOGY

The most common complaint for which the patients sought medical help was upper abdominal pain and discomfort (90%) followed by post prandial fullness (78%). The duration of symptoms ranged between three months to six years. Out of the 224 patients, 102 patients (45.5%) presented within 3-6 months of onset of symptoms. The mean duration of symptoms was 15.3±14.7months. About 50% of patients gave a history of multiple dyspeptic symptoms which implies that none of the symptoms are pathognomonic for a particular condition. No particular symptom was specifically associated with H.pylori positivity.

TABLE 7: DURATION OF SYMPTOMS

Duration of symptoms (in months)	**Cases**	
	No.	%
Up to 6	102	45.5
7 – 12	49	21.9
13 – 24	36	16.1
> 24	37	16.5
Mean **S.D.**	**15.3** **14.7**	

Forty two` patients (18%) had one or more alarm symptoms already mentioned which was more prevalent in patients above 50 years age group. 13 out of 48 patients (27.1%) in the >60 yrs age group had alarm symptoms.

TABLE 8

ALARM SYMPTOMS AND AGE

Age (in years)	Alarm Symptoms			
	Present		Absent	
	No.	%	No.	%
Less than 30 (38)	5	13.2	33	86.8
30-39 (56)	3	5.4	53	94.6
40-49 (44)	11	25	33	75
50-59 (38)	10	26.3	28	73.7
60 & above (48)	13	27.1	35	72.9
Mean S.D.	50.14 14.59		43.49 14.38	
'p'	0.0095 Significant			

The value obtained was statistically significant (p=0.0095) implying that alarm symptoms were more with increasing age.

There was no correlation between the alarm symptoms and gender, duration of disease or socioeconomic status.

Out of the 29 smokers, 10 (34.5%) had one or more alarm symptoms whereas alarm symptoms were absent in 84% of non smokers.

TABLE 9

ALARM SYMPTOMS VERSUS SMOKING STATUS

Smoking among males (135)	**Alarm Symptoms**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Yes (29)	**10**	**34.5**	**19**	**69.5**
No (106)	**17**	**16**	**89**	**84**
'p'	**0.0284 Significant**			

There was a direct correlation between smoking and alarm symptoms (p=0.0284).

Endoscopic findings were analyzed and tabulated in order as shown in table 12. Duodenal ulcer was found in 17 (7.5%) patients, tumor/mass lesion in 9 (4.8%), non specific inflammation in the form of gastritis, duodenitis, esophagitis in 13 (5.8%), and normal study in 173 (77.2%) and other non specific findings in eight (3.5%) patients.

TABLE 10

ENDOSCOPIC FINDINGS

	Ulcer	**Tumor**	**Gastritis**	**Normal**	**others**
MSES	**3**	**7**	**13**	**90**	**5**
LSES	**14**	**2**	**4**	**83**	**3**
TOTAL	**17**	**9**	**13**	**173**	**8**
%	**7.5**	**4**	**5.8**	**77.2**	**3.5**

Prevalence of ulcer was more in the lower socioeconomic status (14 out of 17) and prevalence of tumor more in middle socioeconomic group (seven out of nine) but the values were not statistically significant.

Correlation between alarm symptoms and endoscopic findings was done using 50 years as the cut off age, since gastric malignancy is considered a rare diagnosis in the <50 age group.

It was found that in the <50 years group, 13 out of 19 patients (68.4%) who had alarm symptoms had significant endoscopic lesions whereas 103 out of 119 patients (86.6%) who did not have alarm symptoms had no lesions on endoscopy. Two patients had gastric carcinoma and both patients had alarm symptoms.

On the other hand, in the >50 years group, 14 out of 23 patients (60.9%) who had alarm symptoms had serious lesions on endoscopy including gastric malignancy. Fifty five out of 63 patients (87.3%) without alarm symptoms had no endoscopic findings.

This suggests that alarm symptoms may have good negative predictive value in both age groups.

The results are summarized in table no 11.

TABLE 11: AGE, ALARM SYMPTOMS AND ENDOSCOPIC CORRELATION

Alarm Symptoms	Endoscopic findings			
	Present		Absent	
	No.	%	No.	%
Less than 50 years (138) Present(19)	13	68.4	6	31.6
Absent (119)	16	13.4	103	86.6
'p'	**0.0001 significant**			
More than 50 years (86) Present (23)	14	60.9	9	39.1
Absent (63)	8	12.7	55	87.3
'p'	**0.0001 Significant**			
Total (224) Present(42)	27	64.3	15	35.7
Absent (182)	24	13.2	158	86.8
'p'	**0.0001 Significant**			

The value was statistically significant for both the age groups (**p=0.0001**) implying that **alarm symptoms correlated well with significant endoscopic findings**. **Patients less than 50 years without alarm symptoms did not have any significant lesions whereas patients>50 years with alarm symptoms had a higher incidence of serious lesions. Thus alarm symptoms can be used to predict serious lesions**.

Presence of H.pylori by the rapid urease test was analyzed amongst various endoscopic groups. Total number of patients who tested positive for H.pylori was 132 out of 224 (58.9%). The results are summarized in table 12.

Amongst the various endoscopic groups, all patients with ulcer tested positive. None of the patients with tumors tested positive for the organism. **102 out of 173 patients (59%) in the NUD group were positive for H.pylori.** There was near equal prevalence of H.pylori in males (45.1%) and females (47.1%) in NUD.

TABLE 12

H.PYLORI POSITIVITY IN ENDOSCOPIC LESIONS

	Ulcer		**Tumor**		**Gastritis**		**NUD**		**others**	
	+	-	+	-	+	-	+	-	+	-
MSES	3	0	0	7	4	9	45	45	2	3
LSES	14	0	0	2	4	0	57	26	3	0
TOTAL	17	0	0	9	8	9	102	71	5	3
%	**100**		**0**		**47**		**59**		**62.5**	

In the middle socioeconomic status, **54 out of 118 (45.8%)** tested positive when compared with the lower socioeconomic status in which **78 out of 108 (73.6%)** were positive,

TABLE 13

H.PYLORI AND SOCIOECONOMIC STATUS

Socio Economic Status	**H.Pylori**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Low (106)	78	73.6	28	26.4
Middle (118)	54	45.8	64	54.2
'p'	**0.0001** **Significant**			

This implies that higher infection rates are seen in lower socioeconomic group. **The difference was statistically significant (p=0.0001).**

Age wise positivity for H.pylori in NUD was analyzed. 29 out of total positives (36%) were in the age group of 30-39 years. The rest was equally distributed among the other age groups. Amongst the different age groups, **25 patients with NUD above the age of 60 (70%) were positive and 29 patients in the age group of 30-39 years (61.7%) tested positive for the organism** indicating a bimodal age distribution.

TABLE 14

AGE WISE POSITIVITY FOR H.PYLORI IN NUD

	18-29y		**30-39y**		**40-49y**		**50-59y**		**>60y**	
	Total	**+**	**Total**	**+**	**Total**	**+**	**Total**	**+**	**Total**	**+**
MSES	12	8	24	19	17	11	12	8	18	11
LSES	18	5	23	10	16	8	16	6	18	14
Total	30	13	47	29	33	19	28	14	36	25
%		**43..3**		**61.7**		**57.7**		**50**		**70**

62% of patients with alarm symptoms had positivity for H.pylori in NUD. Most of them (85%) had ulcer like dyspepsia and the rest had dysmotility like dyspepsia but association was not statistically significant.

Out of 29 smokers, 24 (82.8%) tested positive for H.pylori.

TABLE 15

H.PYLORI IN SMOKERS

Smoking among males (135)	**H.Pylori**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Yes (29)	24	82.8	5	17.2
No (106)	59	55.7	47	44.3
'p'	**0.012** **Significant**			

The association between the two variables was statistically significant (p=0.012), implying higher infection rates amongst smokers.

Histopathological findings of the biopsied specimen from three major sites were analyzed in relation to positivity of H.pylori in NUD patients. The findings are summarized in table 16.

TABLE 16

HISTOPATHOLOGICAL FINDINGS IN NUD

	N		**AG**		**BG**		**FG**		**PG**		**LF**		**IM**	
RUT	+	-	+	-	+	-	+	-	+	-	+	-	+	-
MSES	4	36	10	5	2	1	5	1	30	12	26	6	3	0
LSES	20	16	24	2	3	1	10	4	16	3	16	1	1	0
Total	24	52	34	7	5	2	15	5	46	15	42	7	4	0
	76		41		7		20		61		49		4	
%	**33.9**		**18.3**		**3.1**		**8.92**		**27**		**21.87**		**1.7**	

N – Normal study

AG – Antral gastritis

BG – Gastritis of the body of stomach

PG – Pan gastritis

FG – Fundal gastritis

LF – Lymphoid follicles

IM – Intestinal metaplasia

The following observations were made in relation to the histopathology of the mucosa in NUD-

1. Out of 173 patients with NUD, 73 patients (33.9%) had no mucosal lesions and the rest 100 patients (66%) had mucosal lesions. Of the 100 patients with lesions, 61 patients had pan gastritis.

2. Thirty out of 118 patients of the middle socioeconomic status with RUT positivity had pan gastritis (38%). In the same socioeconomic group, a total of 32 patients had formation of intramucosal lymphoid follicles, compared to 17 in the lower socioeconomic status.

3. Isolated antral gastritis was more in lower socioeconomic status (n=24) than the middle socio economic status (n=10).

4. Isolated fundal gastritis was present in a larger number in lower socioeconomic status both in RUT positive (n=10) and RUT negative patients (n=4).

5. Four patients had antral gastritis with intestinal metaplasia and all four were positive for H.pylori, out of which two patients were in the age group <50 years.

6. The presence of lymphoid follicles correlated well with longer duration of disease, as it was seen that 17 out of 37 patients (45.9%) with long duration of symptoms (lasting >24 months) had presence of lymphoid aggregates in mucosa. **The value was statistically significant (p=0.0001).**

TABLE 17

DURATION OF SYMPTOMS VERSUS PRESENCE OF LYMPHOID FOLLICLES

Duration of symptoms (in months)	**Lymphoid Follicles**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Up to 6 (102)	10	9.8	92	90.2
7 – 12 (49)	13	26.5	36	73.5
13 – 24 (36)	9	25	27	75
> 24 (37)	17	45.9	20	54.1
Mean S.D.	23.27 16.96		13.07 13.18	
'p'	**0.0001 Significant**			

TABLE 18

SITE OF GASTRITIS AND LYMPHOID FOLLICLES

Site of Gastritis	Lymphoid Follicles			
	Present		Absent	
	No.	%	No.	%
AG (53)	19	35.8	34	64.2
BG (3)	1	33.3	2	66.7
FG (20)	1	5	19	95
PG (63)	28	44.4	35	55.6

Lymphoid follicles were almost equally distributed at all sites in the stomach.

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Out of 42 patients who had one or more alarm symptoms, 36 patients (85.7%) had significant mucosal lesions.

TABLE 19

ALARM SYMPTOMS VERSUS HISTOPATHOLOGY

Alarm Symptoms	**Histopathological findings**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Present (42)	36	85.7	6	14.3
Absent (182)	111	61	71	39
'p'	**0.0042** **Significant**			

There was good correlation between alarm symptoms and histopathological findings. The value was statistically significant (p=0.0042).

The relation between H.pylori positivity and histopathology of gastric mucosa in NUD was analyzed. Out of 100 patients with mucosal lesions in NUD, 83 of them (81.4%) tested positive for H.pylori.

TABLE 20

CORRELATION BETWEEN HISTOPATHOLOGY AND H.PYLORI POSITIVITY IN NUD

RUT findings among normal Endoscopy cases (173)	**Histopathological findings**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Positive (102)	83	81.4	19	18.6
Negative (71)	17	23.9	54	76.1
'p'	**0.0001 Significant**			

The correlation between the two variables was found to be statistically significant (p=0.0001).

Forty nine patients with NUD (21.9%) had lymphoid follicles in our study. Out of these, 42 patients tested positive for H.pylori.

TABLE 21

LYMPHOID FOLLICLES VERSUS H.PYLORI STATUS

RUT findings among NUD cases (173)	**Lymphoid Follicles**			
	Present		**Absent**	
	No.	**%**	**No.**	**%**
Positive (102)	42	31.4	60	68.6
Negative (71)	7	7	64	93
'p'	**0.0001 Significant**			

Significant correlation was found between the presence of lymphoid follicles and H.pylori positivity in NUD (p=0.0001).

DISCUSSION

Dyspepsia is a common symptom with an extensive differential diagnosis and a heterogeneous pathophysiology. Since dyspepsia affects large numbers of people across a broad spectrum of symptoms, it is not practical to perform endoscopy in all patients with dyspepsia. The appropriate role of endoscopy in the evaluation of dyspepsia is both a pragmatic concern for the gastroenterologist and an important determinant in healthcare costs. This study on the evaluation of upper GI endoscopy in dyspepsia was mainly done to assess the usefulness of endoscopy in patients presenting with new onset dyspeptic symptoms and to study the relation between H.pylori and non ulcer dyspepsia.

Most of the observations made in this study correlated well with world literature. Several studies done in the past have suggested that routine upper gastrointestinal endoscopy for a younger patient with dyspepsia is not indicated as the initial diagnostic procedure.[8,9,13,35,36,37] The most common endoscopic finding in our study was non ulcer dyspepsia (77.2%). The incidence of gastric malignancy is generally low in patients below the age of 50 and this has been observed in several studies in past. Similarly, in our study, the overall incidence of gastric malignancy was low and even lower in patients below the age of 50 years. Only two patients below the age of 50

years had malignancy and both these patients had significant alarm symptoms to indicate the seriousness of the lesion.

The importance of alarm symptoms is evident from the fact that they correlated very well with the presence of serious endoscopic lesions (p=0.0001). They had good negative predictive value in patients < 50 years. This was in accordance with the previous studies done by Johannesen et al[8] and Mansi et al[9] in which the authors found a good negative predictive value of alarm symptoms (97%). Conversely, a significant proportion of patients >50 years with serious endoscopic lesions had one or more alarm symptoms. Alarm symptoms can safely be used to decide which group of patients need endoscopy (p=0.0001). This is in concordance with the large study done by Williams et al in 1988 which suggested that endoscopy may not needed in patients under the age of 45 years.[13] It is neither cost effective nor diagnostic. On the other hand, detailed evaluation of symptoms and physical signs can help to decide which groups of patients need endoscopic evaluation.

The diagnostic workup for dyspepsia in the recent past has been dominated by initial testing for H.pylori and its eradication, bearing in mind the fact that it is strongly associated with most gastroduodenal disorders including non ulcer dyspepsia. This has been highlighted by three recent

major trials which have compared endoscopy with HP testing (Veldhuyzhen et al[35], Zagari et al[36], and Mahadeva et al[37]). All the three trials have proved that endoscopy is not a cost effective procedure as compared to HP test and treat. The yield from endoscopy for patients below 50 years was very low. A non invasive approach to the diagnosis of H.pylori is preferred.

There was similar correlation with regard to prevalence of H.pylori. There have been several studies published in India and the West which have tried to analyze the importance and prevalence of H.pylori in various gastric lesions. Our study reports a prevalence rate of 59% in non ulcer dyspepsia which compares well with world literature. The prevalence rates are summarized in the following table.

Clinical condition	**World figures[1]**	**Our study**
Duodenal ulcer	95-98%	100%
Gastritis	50-65%	47%
Non ulcer dyspepsia	**50-60%**	**59%**
Gastric carcinoma	six fold increase	0%

There was a higher prevalence of the infection in the lower socioeconomic status (p=0.0001) and this is consistent with the epidemiology of the infection. This was previously demonstrated in a

population study performed by Paul Moayeddi et al in the United Kingdom which found significant correlation between H.pylori and poor living conditions.[38] There was no particular sex predilection in past studies and similar results were obtained in our study too.[38] There was almost equal prevalence of infection in males (45.1%) and females (47.1%). No specific symptom correlated with the presence of H.pylori in our study and this fact has been well emphasized in the past also.

The etiology of non ulcer dyspepsia remains elusive. Most researchers believe that there is a relation, although an imperfect one, between non-ulcer dyspepsia and infection with H.pylori. The pathophysiological mechanisms by which the infection may cause dyspepsia are unclear, but may include changes in acid secretion, abnormal motility, or altered visceral perception. The association of non ulcer dyspepsia with H. pylori infection has been widely reported in the recent past.[24,38,39,40] However, the issue of whether this relation is causal or casual still remains debatable.

Several studies have assessed the epidemiological association between H. pylori infection and non ulcer dyspepsia. There was good correlation of our findings with the previous studies in India on non ulcer dyspepsia and its relation to H.pylori. These studies showed a peak age prevalence of between 30-39 years. A slight variation was observed in this

study in that there was a bimodal distribution of H.pylori (30-39 years, >60 years). This could probably be explained by the fact that Helicobacter infection increases with age and also to increased longevity. The previous study done in Madurai by Thayumanavan et al reported a prevalence rate of around 50.3% in non ulcer dyspepsia.[24]

	GILL ET AL[39]	KHANNA ET AL[40]	THAYUMANAVAN ET AL[24]	Our study
Prevalence	46 %	74 %	50.3%	59%
Age group	20 - 40	-----	30-40	Bimodal 30-39 >60 yrs

There was a significant correlation between smoking and presence of H.pylori infection (p=0.012) in our study. Nearly 83% of smokers were infected. Previous studies have also indicated that smoking is a significant risk factor for H.pylori infection. A study done by Murray et al in Northern Ireland analyzed the relation of H.pylori to smoking and alcohol and showed that the prevalence of H.pylori was higher in smokers and ex smokers.[41]

In our study, we studied the histopathology of the gastric mucosa in non ulcer dyspepsia to see if there were any significant lesions. Studies on

the histology of non ulcer dyspepsia are lacking and there is very limited information available. There are no large scale studies in India. The findings in our study correlated well with the previously done studies. Out of 173 patients with non ulcer dyspepsia, 117 patients (68%) had significant mucosal lesions including lymphoid aggregates and intestinal metaplasia. One study done in Nigeria by Sylvester et al showed that a significant proportion of patients with non ulcer dyspepsia (70%) had gastric mucosal lesions.[32] A similar study was done by Schade et al and also demonstrated the need for further evaluation of the mucosa in non ulcer dyspepsia.[42]

A significant proportion of patients with gastric lesions had evidence of H.pylori infection (p=0.0001). Among the patients who had mucosal lesions, 81.4% of patients were positive for H.pylori. This has been well emphasized in the study done by Sylvester et al.[32] This indicates that H.pylori could be responsible for the dyspeptic symptoms and the mucosal lesions in the stomach.

Lymphoid follicles in the gastric mucosa represent a common response to H. pylori infection. The range of this response varies from 27% to 100% in previous publications.[32,43,44,45] Previous studies have concluded that the presence of lymphoid follicles in the gastric mucosa appears to be a strong predictor of H. pylori infection. The importance of lymphoid

transformation of the gastric mucosa has been well stressed in a retrospective study of gastric mucosal biopsies done by Mohammed Afzal et al in Saudi Arabia which found a significant correlation between lymphoid follicles and presence of H.pylori infection. In this study nearly 95% of patients with lymphoid follicles had evidence of H.pylori infection.[45]

They concluded that finding even a single lymphoid follicle in a gastric biopsy specimen is associated with a very high probability (>90%) of detecting H. pylori in the same or in another synchronous biopsy specimen obtained from that patient.

There were similar observations made in our study. Forty nine patients with NUD in our study had lymphoid aggregates in the gastric mucosa out of which 42 (85.4%) were positive for H.pylori. There was a significant relation between the presence of lymphoid aggregates and H.pylori infection in our patients (p=0.0001) and there was also significant correlation between the duration of symptoms and presence of lymphoid aggregates (p=0.0001). More than 50% of the patients with lymphoid follicles had a long duration of symptoms. This probably reflects the chronicity and severity of the lesions despite the presence of normal endoscopy, placing these patients at risk of the indolent gastric MALT lymphoma.

Our study supports the conclusion derived from the study done by Mohammed et al.[45] The conclusion derived from that study was that lymphoid follicles are absent in the normal stomach, therefore their appearance in the stomach with H. pylori associated gastritis, is an issue of considerable interest. The development of mucosa associated lymphoid tissue is a necessary first step in the development of primary MALT lymphoma in various organs such as lung, thyroid or stomach that are normally devoid of MALT . Therefore, association in the stomach mucosa suggests a causal relationship between H. pylori and the origin of gastric MALT lymphoma. The present study supports other reports that H pylori infection may be directly related to the development of gastric MALT lymphoma. This provides the necessary background where other as yet unidentified factors may act leading to the development of lymphoma in a small proportion of cases. Also it supports the concept that eradication of H. pylori results in prevention or regression of previously developed MALTOMA of the stomach which has been emphasized in the past.[1,2] Further controlled studies and therapeutic trials would help further clarify this relationship.

In a retrospective study done by Ghoshal et al in Indian patients with gastric lymphomas, it was found that these patients had repeatedly normal

endoscopies and the diagnosis was achieved only on gastrectomy.[50] Furthermore, there was a very strong association between gastric lymphomas and H.pylori. Our study has shown significant gastric lymphoid aggregates despite normal endoscopy. Lymphomas evade diagnosis most of the times requiring high degrees of suspicion. They must be identified early because they are completely curable in early stages. It may be worth subjecting these patients to eradication therapy to prevent malignancy in future.[46, 47, 48, 49] Jakkimeinen et al showed that H.pylori was associated with a significant number of cases of non ulcer dyspepsia and eradication produced reasonable symptomatic benefit in these patients.[48] There was similar observation made by Paul Moayyedi et al in a meta analysis.[46] There are no large scale follow up studies to study the status of the mucosa on follow up and the very few early studies have suggested further evaluation of the mucosal status.[43, 44, 45]

The association between H.pylori and gastric carcinoma was negligible in our study consistent with past Indian studies. None of the patients with malignancy tested positive for H.pylori. It has been referred to as the Indian enigma. The study done by Ghoshal et al concluded that H.pylori prevalence was not significantly different amongst patients with carcinoma and controls. Indian patients were also found to have less

incidence of gastric cancer despite the high prevalence of H.pylori infection, thus raising doubts about the direct association of H.pylori infection with gastric adenocarcinoma. The reason quoted is the presence of some genetic, dietary or environmental factors which have a protective effect against the development of malignancy. This has not been proved to date and needs further evaluation.[50]

It may be worth performing a triple site mucosal biopsy for early identification of lymphoid infiltration into the stomach. Patients with gastric lymphoid aggregates may have to be subjected to immunological studies to detect the presence of low grade MALT lymphomas. Further follow up of these patients is needed to find the response rates.

SUMMARY

The study “Evaluation of upper gastrointestinal endoscopy in with special reference to Helicobacter pylori in non ulcer dyspepsia” was a cross sectional study of 224 patients admitted with new onset dyspepsia in Government Rajaji Hospital, Madurai.

Patients who satisfied the inclusion criteria were interviewed for dyspeptic symptoms and alarm symptoms. They underwent investigations like ultrasonography, upper gastrointestinal endoscopy and tissue urease test for H.pylori with mucosal biopsy. The correlation between alarm symptoms, endoscopic findings and histopathological findings was analyzed. Patients without alarm symptoms did not have serious lesions on endoscopy or histopathology. There was high prevalence of H.pylori in lower socioeconomic population and smokers. Significant mucosal inflammatory lesions were present on histopathological examination in patients with normal endoscopy but positive for H.pylori.

This study highlights the fact that endoscopy is not warranted in patients <50 years with new onset dyspepsia and without alarm symptoms. Testing for H.pylori is needed in all patients with dyspepsia and histopathology of mucosa may be required in patients who test positive for H.pylori for early detection of lymphoid transformation in the stomach.

CONCLUSIONS

1. There was significant correlation between alarm symptoms and gastric lesions in dyspepsia; hence endoscopy is recommended for these patients.

2. In patients aged <50 years without alarm symptoms, endoscopy did not reveal any lesions. Hence endoscopy may not be needed routinely in these patients; they can be managed with the “treat first, test later” approach.

3. H.pylori was prevalent in 60% of patients with NUD and was comparable with world literature.

4. H.pylori prevalence was highest in 4^{th} to 7^{th} decade.

5. H.pylori prevalence was significantly higher in the lower socioeconomic status.

6. Smoking is a significant risk factor for H.pylori.

7. H.pylori positivity was associated with significant mucosal lesions including lymphoid follicles and intestinal metaplasia despite normal endoscopy; hence routine biopsy of the mucosa is needed.

8. The initial concept of ignoring H.pylori in non ulcer dyspepsia may have to be redefined since many patients in our study had significant mucosal lesions.

9. Further immunological studies may be needed to evaluate patients with lymphoid follicles to detect the presence of low grade MALToma.

APPENDIX

Bibliography

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PROFORMA

S.NO.

NAME AGE: SEX:

ADDRESS: UNIT: WARD:

OP/IP NO:

Occupation:

Educational status:

Monthly income:

Socioeconomic status score:

SOCIOECONOMIC STATUS:

COMPLAINTS	DURATION
1. Upper abdominal pain	
2. Abdominal discomfort	
3. Bloating sensation	
4. Early satiety	
5. Post prandial fullness	

ALARM SYMPTOMS	DURATION
1. Dysphagia	
2. Upper GI bleed (hematemesis/melena)	
3. Persistent vomiting	
4. Sensation of an abdominal mass	
5. Jaundice	
6. Loss of weight	
7. Loss of appetite	

PAST HISTORY:

Systemic illness:

Drug intake: (antibiotics/ PPI/metronidazole/NSAIDs/others)

Prior endoscopy: Y/N

PERSONAL HISTORY:

Alcohol intake: Y/N Smoking: Y/N

Betel chewing: Y/N

EXAMINATION:

Nutritional status: oral hygiene: good/poor

Anemia: Y/N jaundice: Y/N

Lymphadenopathy: Y/N

Abdomen: epigastric tenderness: Y/N

Abdominal mass: Y/N

INVESTIGATIONS:

1. Blood urea (mg/dl):
2. Serum creatinine (mg/dl):
3. Hemoglobin (grams/dl):
4. ESR (mm in 1 hour):
5. Ultrasonography of abdomen:

6. Upper GI endoscopy:

7. Rapid urease test: +/-
8. Biopsy findings:

FIGURE 1: DISCOVERERS OF H.PYLORI: BARRY MARSHALL AND WARREN

FIGURE 2: RELATION OF H.PYLORI TO GASTRIC MUCOSA

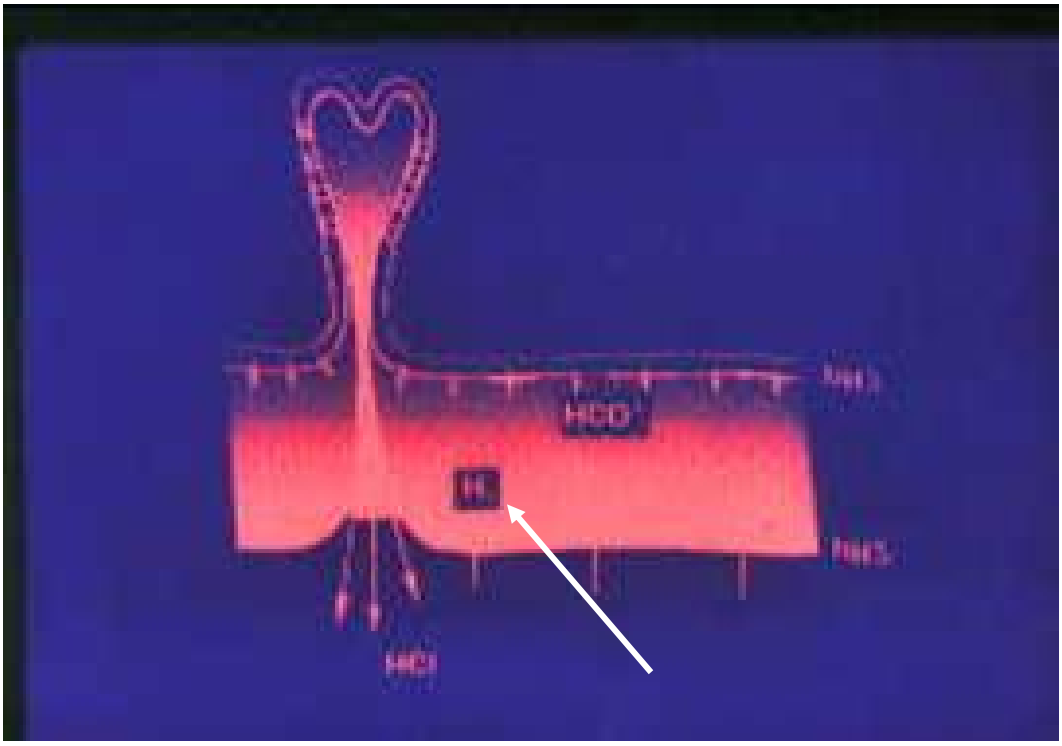


FIGURE 3: GASTRIC MUCOSA: HISTOPATHOLOGY AND H.PYLORI

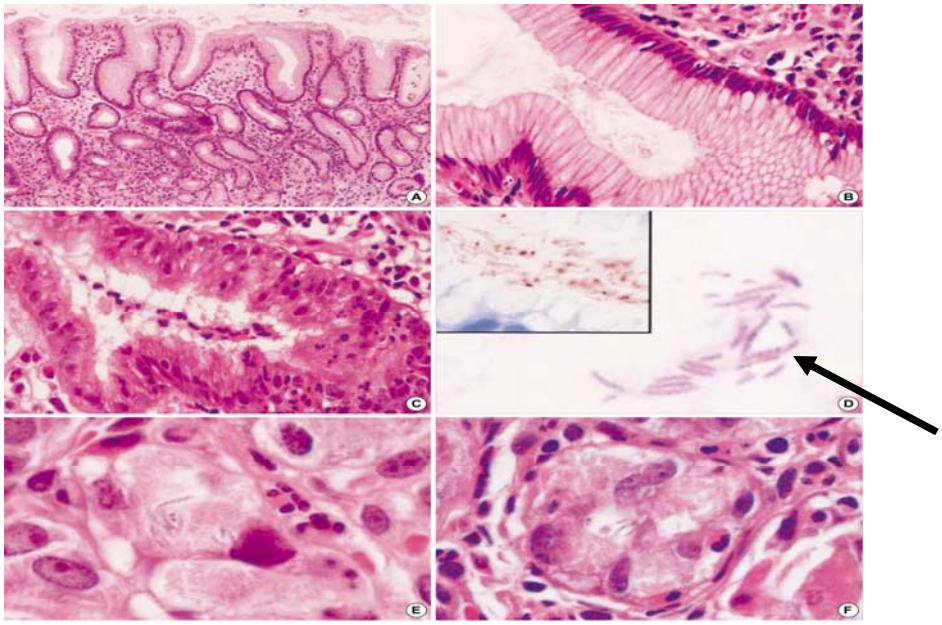


FIGURE 4: GASTRIC INTRAMUCOSAL LYMPHOID AGGREGATES

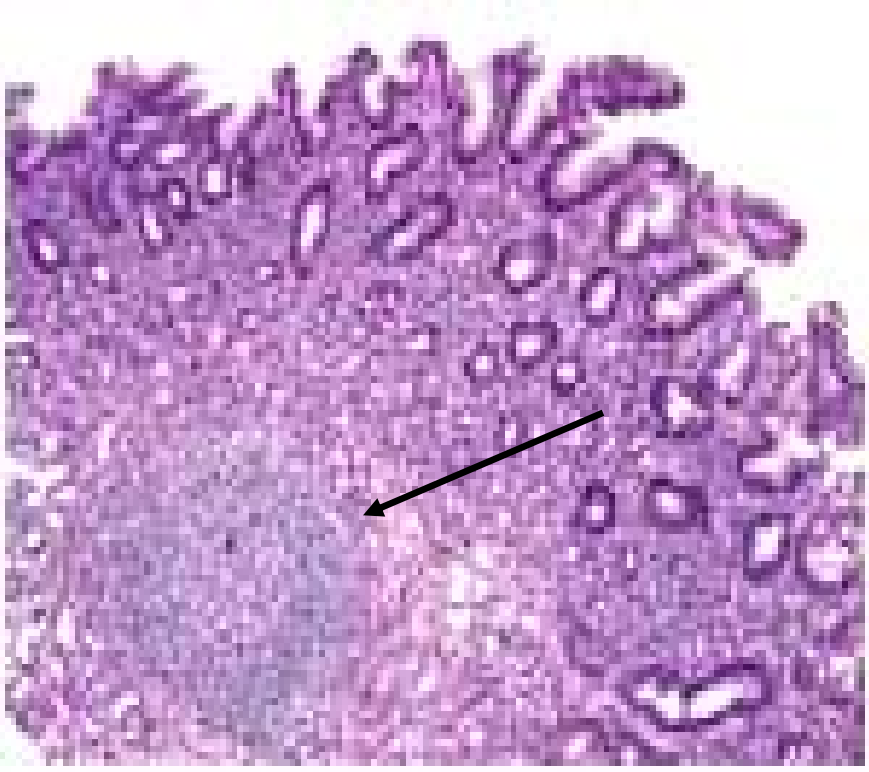


FIGURE 5: THE ULTRA RAPID UREASE REACTION

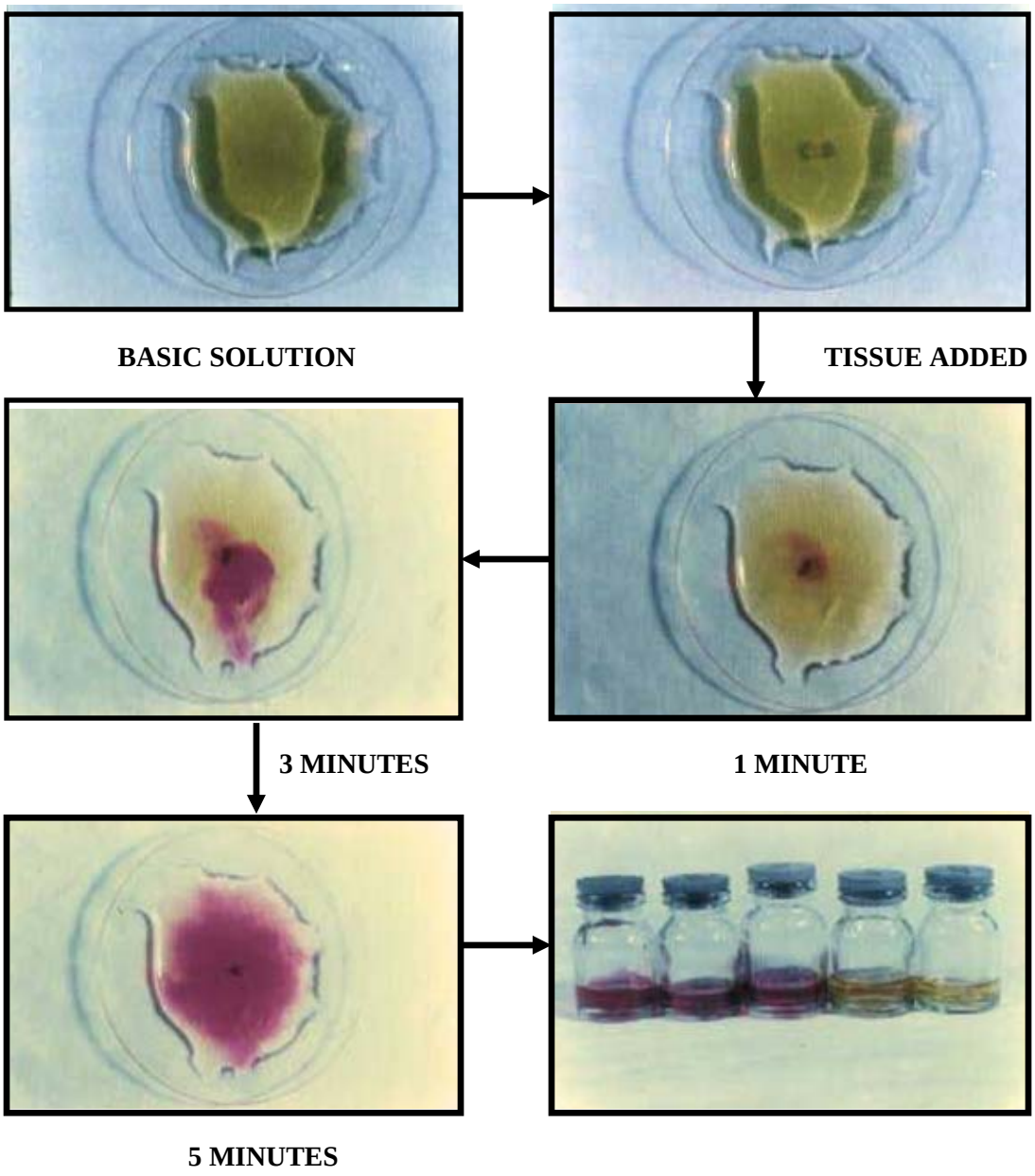


FIGURE 6: AGE DISTRIBUTION

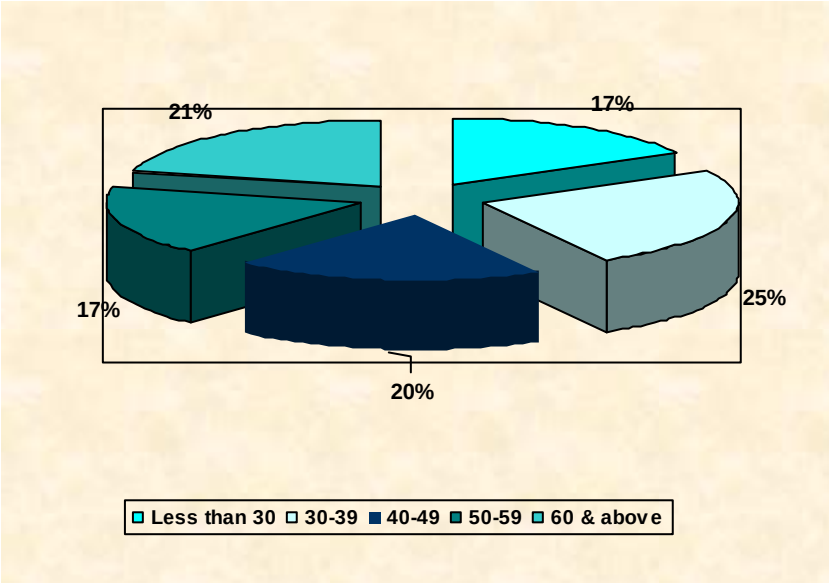


FIGURE 7: SOCIOECONOMIC STATUS

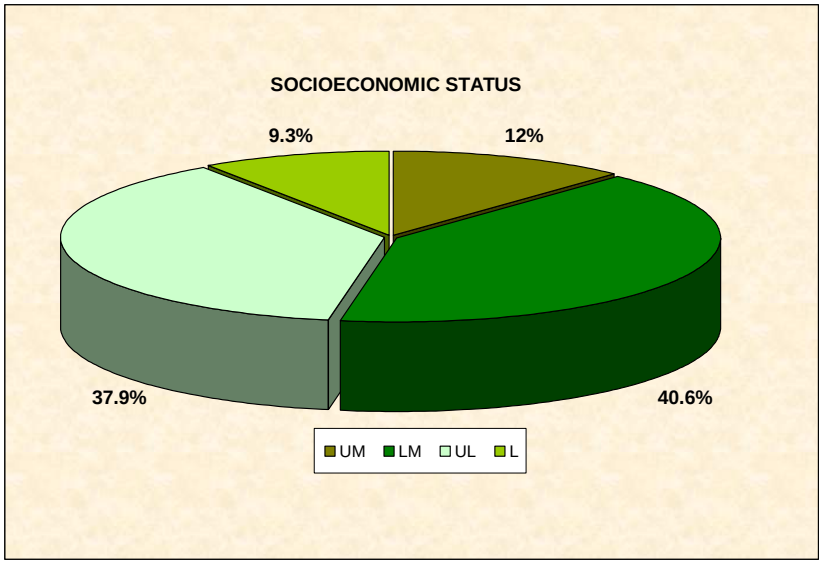


FIGURE 8: ENDOSCOPIC FINDINGS

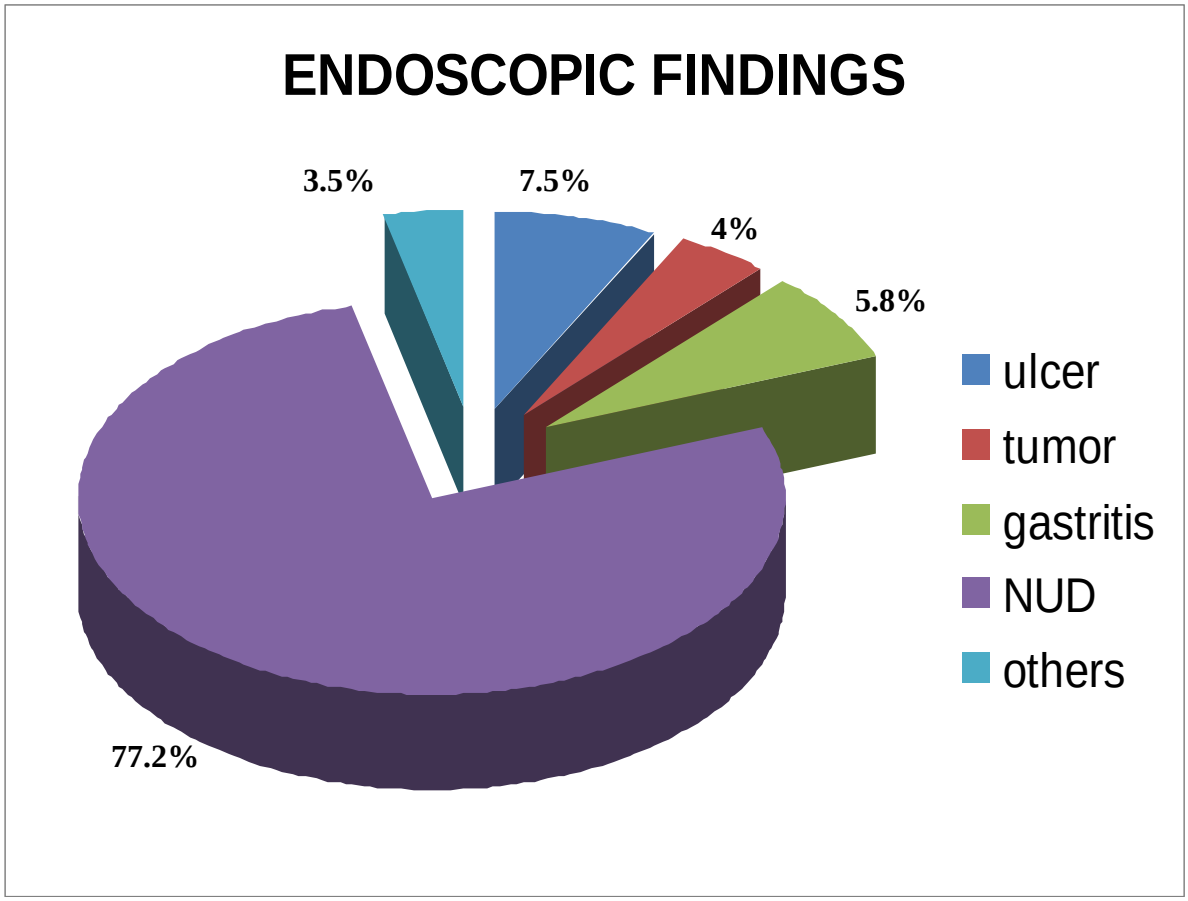


FIGURE 9: ALARM SYMPTOMS AND ENDOSCOPIC CORRELATION

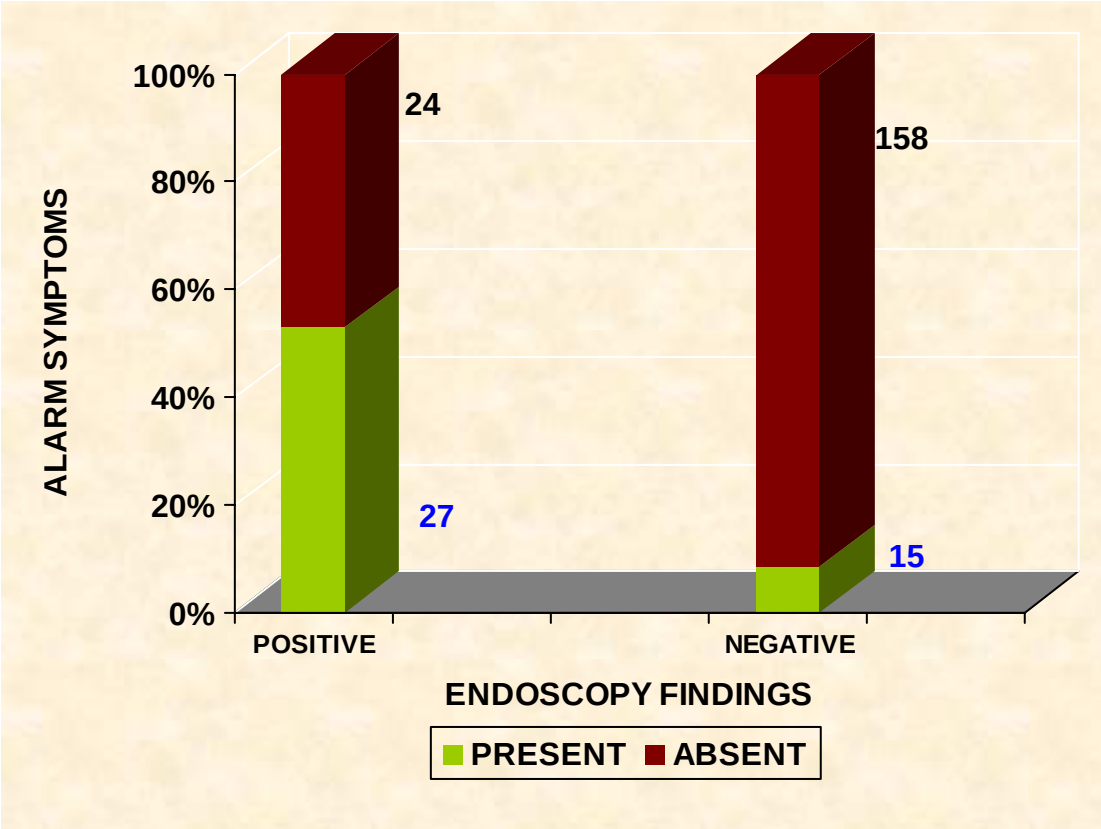


FIGURE 10: H.PYLORI AND SOCIOECONOMIC STATUS

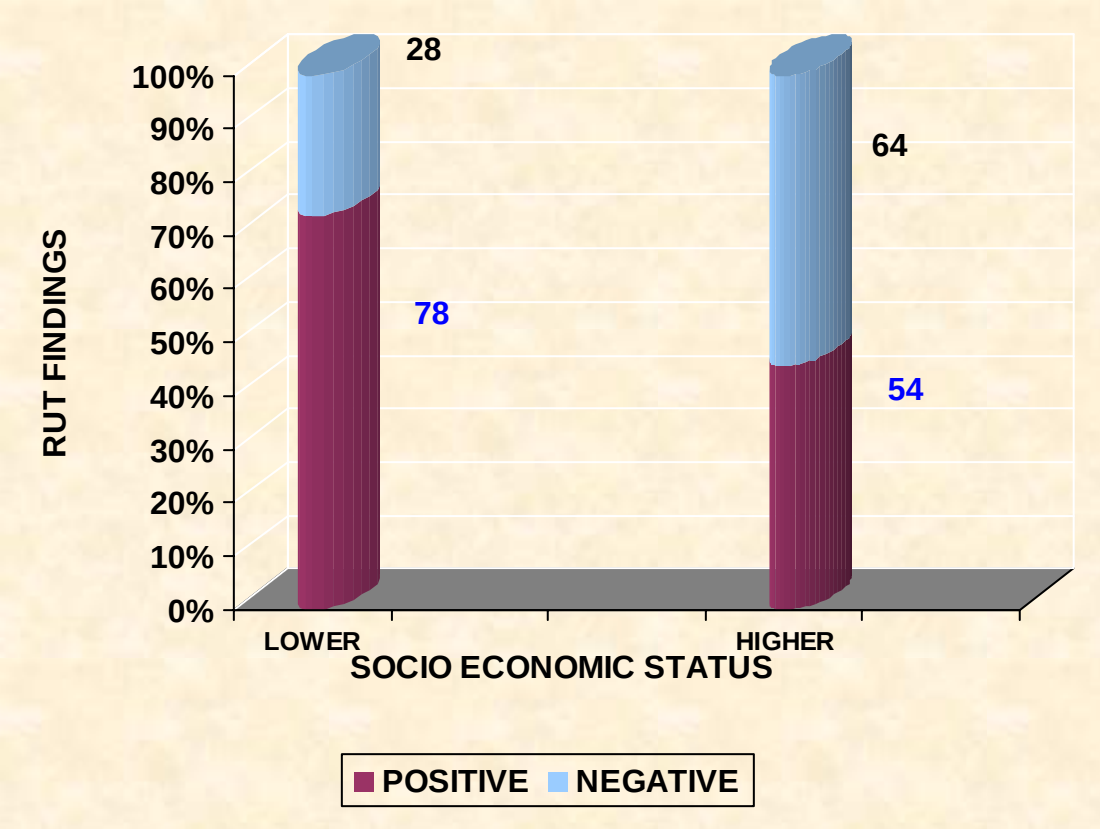


FIGURE 11: H.PYLORI AND SMOKING STATUS

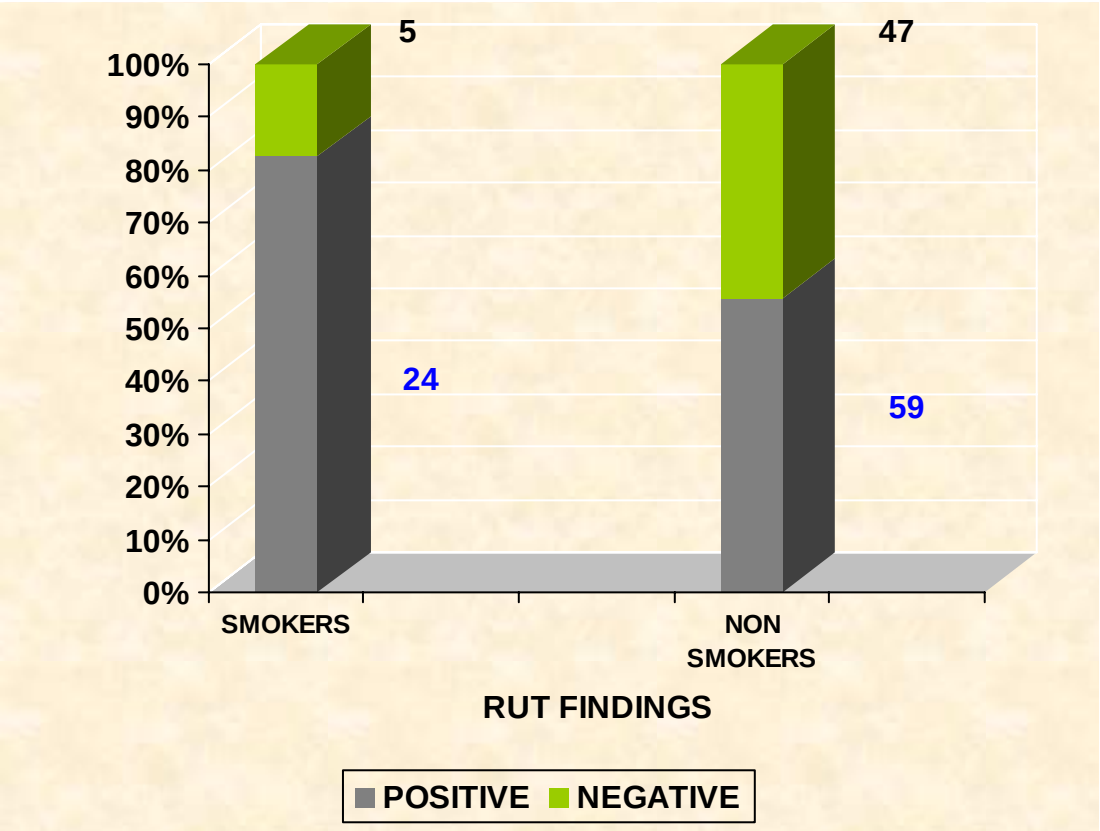


FIGURE 12: HISTOPATHOLOGICAL FINDINGS IN RUT POSITIVE NUD PATIENTS

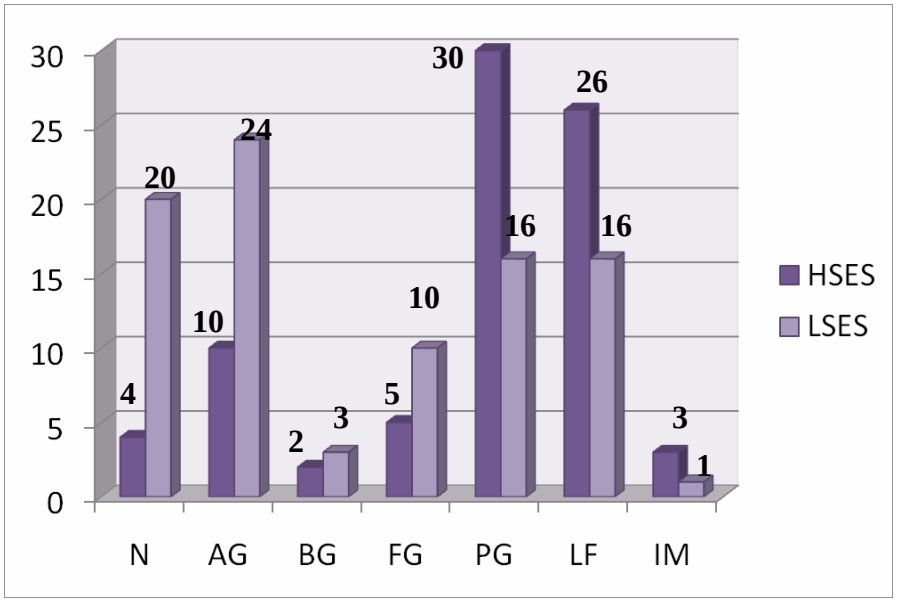


FIGURE 13: HISTOPATHOLOGICAL FINDINGS IN RUT NEGATIVE NUD PATIENTS

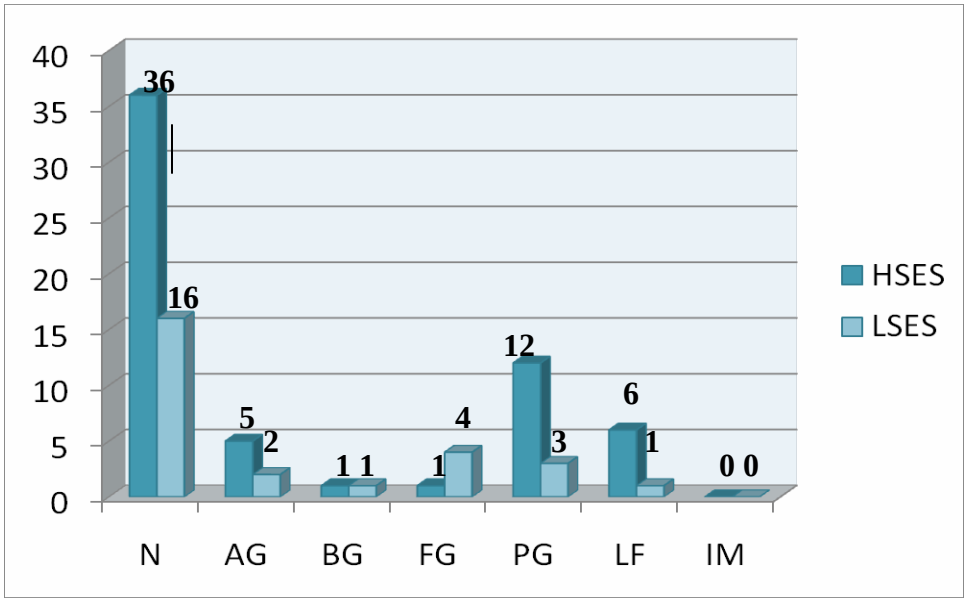


FIGURE 14: DURATION OF SYMPTOMS VERSUS LYMPHOID FOLLICLES

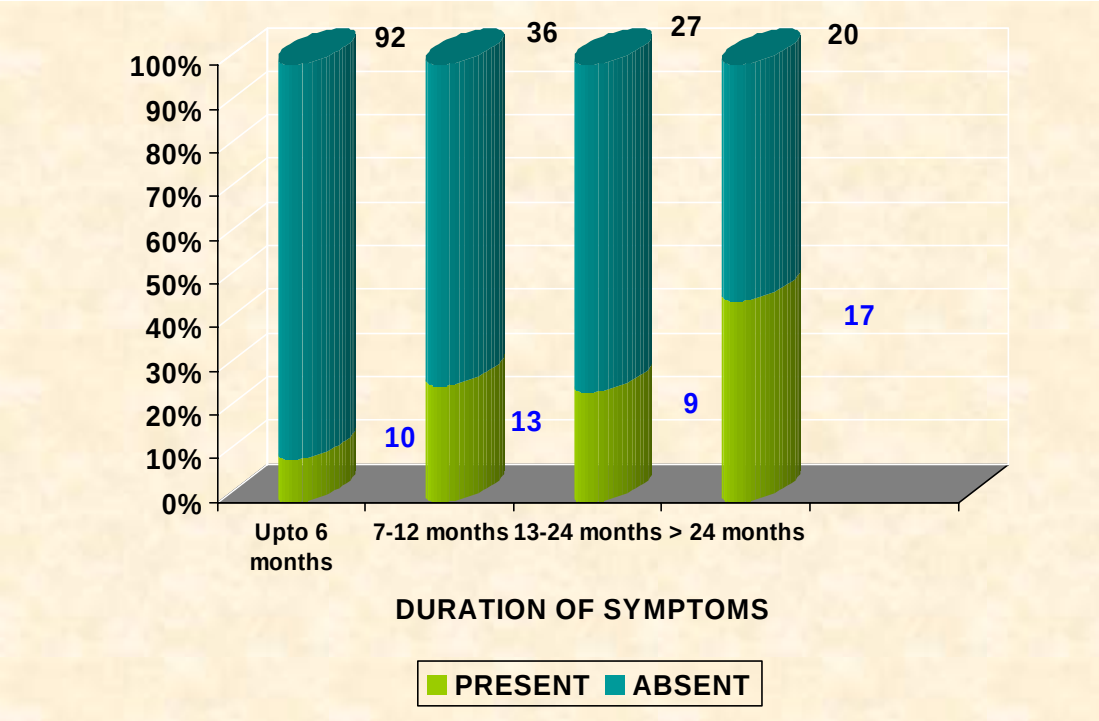


FIGURE 15: H.PYLORI VERSUS HISTOPATHOLOGICAL LESIONS IN NUD PATIENTS

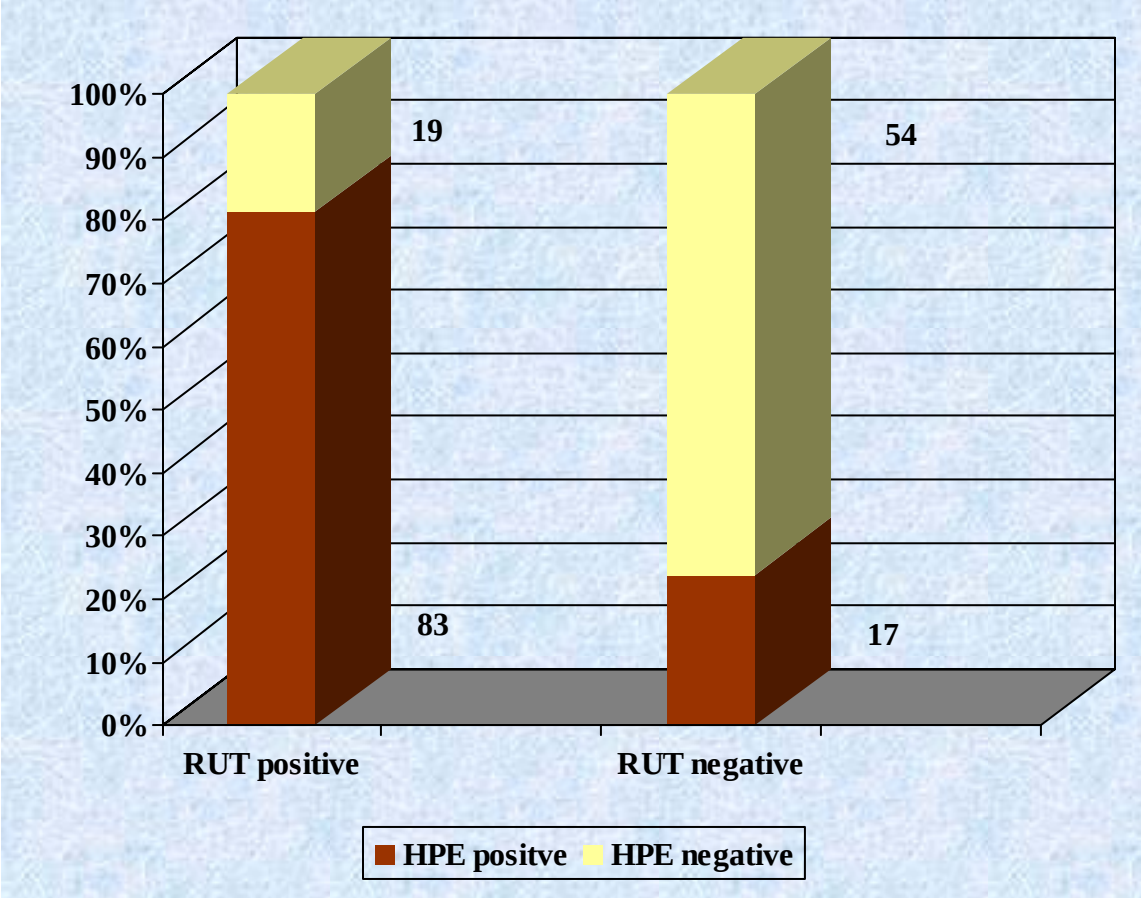
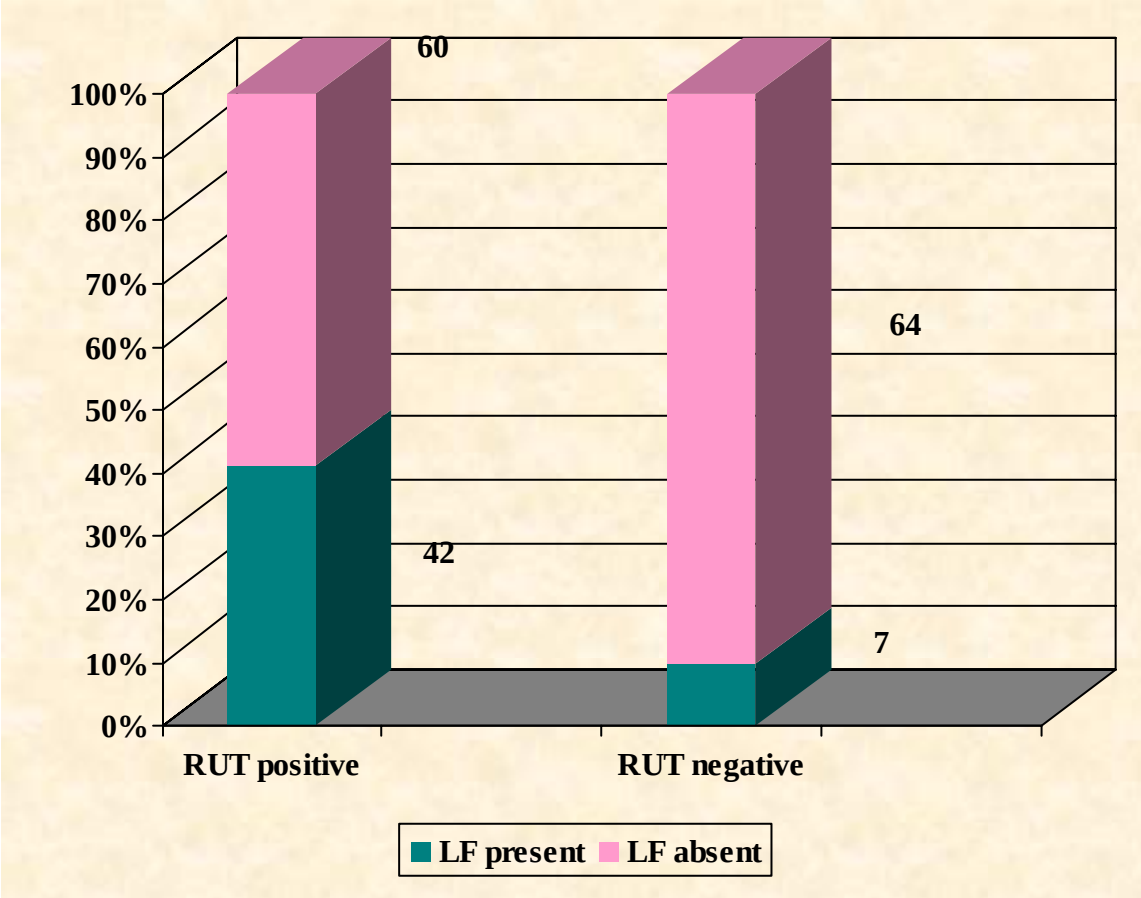


FIGURE 16: H.PYLORI VERSUS LYMPHOID FOLLICLES



MASTER CHART

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
LOWER SOCIOECONOMIC STATUS																
1	32	M	4	L	6m	N	N	n	10.6	20	0.8	10	n	n	+	n
2	28	F	6	UL	8m	N	N	n	9.8	19	0.7	15	n	n	-	FG
3	48	M	7	UL	18m	Y	Y	n	11.6	40	1.2	15	n	n	-	n
4	24	M	6	UL	6m	N	N	n	12	24	0.6	10	n	n	-	n
5	23	M	6	UL	3m	N	Y	n	12.8	32	0.8	18	n	n	+	AG
6	35	F	6	UL	24m	N	N	n	11.4	20	1	22	n	n	+	n
7	45	M	7	UL	6m	N	Y	n	12	34	0.9	20	n	n	+	AG
8	42	F	7	UL	3m	N	N	et	10	18	0.8	14	n	n	+	FG
9	18	F	4	L	3m	N	N	n	11	18	0.9	20	n	n	+	AG
10	35	F	7	UL	12m	N	N	n	11	17	0.9	20	n	n	+	AG
11	43	M	4	L	12m	Y	Y	et	11.8	28	1	22	n	n	+	PG
12	40	M	8	UL	12m	N	N	et	11.4	18	0.9	5	n	n	+	BG
13	32	M	9	UL	8m	Y	Y	et	10.2	20	0.9	20	n	ADU	+	n
14	20	M	10	UL	6m	N	N	n	10.8	18	0.9	15	n	n	+	PG
15	39	F	4	L	10m	N	N	n	12	17	0.7	20	n	n	-	n
16	45	M	9	UL	3m	N	Y	n	11.4	17	0.8	5	n	n	+	AG
17	75	M	4	L	3m	N	N	et	9.8	22	1.1	22	n	DUO	+	PG
18	19	M	8	UL	12m	N	N	n	10	22	0.9	10	n	n	-	n
19	70	F	7	UL	12m	Y	N	n	9.2	45	1.2	25	n	n	+	AGLF
20	25	F	8	UL	3m	Y	N	n	7.6	28	0.9	28	n	DUO	+	PG
21	26	M	9	UL	24m	N	Y	et	10.2	30	1.1	18	n	DU	+	AG
22	55	M	10	UL	3m	Y	Y	et	9.6	34	1.2	28	n	DB	+	AG
23	43	F	3	L	3m	N	N	et	11	28	1.1	30	n	EG	+	FG
24	21	M	7	UL	3m	N	N	et	11.8	23	1	22	n	n	+	n
25	30	M	6	UL	36m	N	N	et	13	30	1	10	n	n	+	AG
26	75	M	9	UL	3m	N	N	et	10.8	20	1.1	20	n	n	+	FG
27	58	M	4	L	3m	N	Y	et	10	30	1.2	24	n	n	+	AG
28	28	F	8	UL	36m	N	N	et	9	34	0.9	36	n	EG	+	FG
29	52	M	9	UL	24m	N	N	n	11.2	34	0.9	10	n	n	+	AG
30	35	F	10	UL	4m	N	N	n	10	18	0.8	22	n	n	-	n
31	45	M	10	UL	24m	N	N	n	11.8	28	0.7	10	n	n	+	AG
32	30	M	8	UL	24m	Y	N	et	11.8	28	0.6	20	n	ADU	+	AG

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
33	30	F	4	L	30m	N	N	et	10	30	1	15	n	n	+	n
34	60	M	7	UL	3m	N	N	et	12.2	38	1.1	10	n	n	+	n
35	30	F	8	UL	3m	N	N	et	9.2	28	0.9	28	n	DU	+	AG
36	37	M	7	UL	4m	N	Y	n	11.2	50	1.8	18	n	FG	-	FG
37	28	M	8	UL	4m	N	Y	et	9.4	28	0.9	10	n	DU	+	AG
38	60	F	9	UL	4m	N	N	et	10.2	21	1	22	n	n	+	PG
39	36	F	9	UL	12m	N	N	et	10	20	0.8	28	n	DU	+	PGLF
40	52	M	4	L	24m	Y	N	et	10	28	0.6	10	n	n	+	AGPG
41	28	M	4	L	3m	N	N	et	10.9	30	1	20	n	CDU	+	AG
42	65	F	10	UL	18m	Y	N	et	9.2	40	1.2	28	n	n	-	FG
43	58	F	10	UL	18m	N	N	et	9.8	42	1	28	n	n	-	FG
44	45	F	9	UL	24m	N	N	et	10	28	1	18	n	n	+	FG
45	45	M	9	UL	3m	Y	Y	et	9	40	1.3	40	n	ADU	+	AGLF
46	24	M	9	UL	6m	N	N	et	10.8	28	1	10	n	n	+	n
47	66	M	4	L	6m	N	N	et	9	40	1.2	40	n	n	+	PG
48	35	M	8	UL	12m	N	N	et	12.8	21	0.8	12	n	n	+	AFIM
49	42	M	8	UL	12m	N	Y	et	10.4	40	1.6	20	n	n	-	BG
50	37	M	4	L	60m	N	N	et	9.2	20	0.6	40	n	n	-	n
51	42	M	6	UL	6m	N	N	et	11.8	38	1	20	n	n	+	AG
52	29	M	6	UL	72m	Y	N	et	9.8	30	1.2	28	n	n	+	PGLF
53	50	F	9	UL	60m	N	N	et	10.8	30	0.9	32	n	n	+	AGLF
54	66	M	9	UL	12m	N	N	et	10	27	0.9	28	n	n	-	FG
55	33	M	4	L	12m	N	Y	et	11	28	0.9	20	n	n	+	n
56	37	M	4	L	3m	N	N	et	12	20	0.6	18	n	n	+	AG
57	49	F	7	UL	4m	N	N	et	10.2	28	0.9	20	n	n	-	PG
58	37	M	4	L	6m	N	N	n	11.5	30	1	40	n	n	+	AG
59	37	M	6	UL	72m	N	Y	et	12	19	0.9	12	n	ADU	+	AG
60	59	F	9	UL	36m	N	N	n	11.7	30	1.2	20	n	n	-	n
61	56	M	9	UL	4m	Y	Y	et	10.2	30	0.8	10	n	n	+	PG
62	54	M	6	UL	3m	N	Y	et	10.4	40	1.2	40	n	n	+	AG
63	60	F	7	UL	36m	N	N	n	9.7	38	1.4	20	n	n	+	PGLF
64	36	F	10	UL	6m	N	N	n	10.6	28	0.9	22	n	n	+	PGLF

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
65	38	F	9	UL	12m	N	N	n	13	18	0.6	18	n	n	+	AGLF
66	52	F	4	L	4m	N	N	n	12.2	40	0.9	22	n	n	+	n
67	60	F	8	UL	4m	Y	N	et	10.8	40	0.9	20	n	n	-	n
68	40	F	8	UL	6m	Y	N	et	11.2	26	0.9	20	n	n	+	FG
69	28	M	6	UL	12m	N	Y	et	11.2	28	0.7	10	n	n	+	BGAG
70	50	F	6	UL	6m	Y	N	et	8.6	42	1	60	n	AGR	-	PDAC
71	26	F	9	UL	12m	N	N	et	11	26	0.9	20	n	n	+	AG
72	56	M	10	UL	6m	N	N	et	11	24	0.7	10	n	n	-	n
73	30	F	9	UL	36m	N	N	n	10	36	1.2	22	n	n	-	PG
74	55	F	9	UL	3m	N	N	n	10	22	0.8	26	n	ADU	+	AG
75	19	F	4	L	12m	N	N	n	11.9	20	0.6	28	n	n	-	n
76	60	F	10	UL	72m	N	N	n	10.8	40	0.9	32	n	n	-	n
77	38	M	9	UL	4m	N	N	n	11.6	30	0.9	22	n	n	+	n
78	60	M	8	UL	24m	Y	N	et	10.8	26	0.9	10	n	DU	+	AGLF
79	62	M	7	UL	12m	N	Y	et	13	29	1.2	26	n	n	+	FG
80	31	M	4	L	7m	N	N	n	10	18	0.9	16	n	n	+	n
81	60	F	8	UL	24m	N	N	n	9.8	40	1.2	28	n	n	+	PGLF
82	46	M	9	UL	36m	N	N	et	10.2	28	0.9	20	n	ER	+	PGLF
83	27	M	10	UL	6m	N	Y	et	11	30	0.9	10	n	DB	+	AGLF
84	32	M	9	UL	36m	N	N	n	12.2	18	0.9	10	n	n	+	n
85	33	M	10	UL	5m	N	N	et	12	24	0.9	24	n	n	+	PG
86	65	M	9	UL	6m	N	N	n	14	23	1	10	n	n	-	n
87	73	F	4	L	24m	N	N	et	9	30	1.2	34	n	n	+	PGLF
88	60	M	4	L	4m	Y	Y	et	8.8	43	0.9	30	n	n	+	n
89	37	M	4	L	3m	N	Y	et	12.9	34	0.9	12	n	n	+	n
90	24	M	9	UL	6m	yes	N	et	13	23	1	10	n	DU	+	AGLF
91	45	F	6	UL	8m	N	N	n	12	19	0.9	15	n	n	+	PGLF
92	35	F	6	UL	12m	N	N	n	13.2	18	1	20	n	n	+	FGAG
93	50	F	7	UL	24m	N	N	n	14	23	0.7	24	FL	n	+	PG
94	42	M	10	UL	36m	N	N	n	12	34	0.9	28	n	n	-	n
95	45	M	9	UL	3m	N	Y	n	12.7	24	1	12	n	n	-	AGLF
96	37	F	8	UL	4m	N	N	n	13.6	23	1	10	FL	n	+	PGLF

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
97	52	F	6	UL	24m	Y	N	n	8.6	42	1.6	105	n	n	-	n
98	47	M	7	UL	10m	N	N	n	12	30	1.2	10	n	n	-	n
99	32	M	10	UL	6m	N	Y	n	13.5	38	0.9	14	n	n	+	BGAG
100	70	M	9	UL	6m	N	N	n	12	23	0.9	34	n	n	-	AG
101	45	F	8	UL	12m	N	N	n	12.5	34	0.7	20	n	n	+	n
102	64	M	9	UL	4m	N	N	n	10	25	1	36	n	n	-	PG
103	62	F	7	UL	36m	N	N	n	10.8	23	1.2	26	n	n	+	AG
104	44	M	6	UL	6m	N	N	n	13	24	1	20	n	HG	+	AG
105	38	M	10	UL	36m	N	N	n	12	26	0.8	34	n	n	-	n
106	45	M	9	UL	48m	Y	N	n	10	34	1	48	n	ND	+	PGLF
MIDDLE SOCIOECONOMIC STATUS																
107	29	F	22	UM	6m	N	N	n	12	19	0.8	20	n	n	-	PG
108	60	M	12	LM	12m	N	N	n	13	28	1	26	n	n	+	n
109	41	F	12	LM	24m	N	N	n	12	28	1.2	20	FL	n	+	PG
110	52	F	14	LM	24m	N	N	et	11.8	18	0.9	22	FL	n	+	n
111	20	F	11	LM	3m	N	N	n	10.8	18	0.8	18	n	n	-	n
112	35	F	12	LM	24m	N	N	n	11	18	0.8	18	FL	n	+	n
113	31	M	15	LM	36m	N	N	et	13	28	1.1	18	n	n	-	n
114	29	F	11	UM	3m	N	N	et	12.8	18	0.6	20	n	n	-	n
115	56	M	12	LM	6m	N	N	n	13.8	38	1.2	12	n	n	-	PG
116	65	F	13	LM	3m	N	N	n	10.8	36	1.2	20	n	n	-	n
117	67	M	14	LM	12m	N	Y	et	9.6	40	1	40	n	n	+	PGLF
118	62	M	11	LM	36m	N	N	n	13	38	1.2	12	n	n	+	PG
119	25	F	15	LM	6m	N	N	n	12.2	24	1	10	n	n	+	AG
120	19	F	19	UM	3m	N	N	n	13	20	0.6	12	n	n	-	n
121	27	F	12	LM	4m	N	N	n	12.3	14	0.7	16	n	n	-	n
122	76	M	11	LM	6m	N	N	n	10	28	1	50	n	n	+	PGIM
123	45	F	15	LM	36m	N	N	n	9.8	30	1	20	n	n	+	PGLF
124	45	M	14	LM	6m	N	N	n	14	38	1.2	18	n	n	-	n
125	67	F	23	UM	8m	N	N	n	9	28	1	40	n	n	+	PG
126	70	M	23	UM	12m	N	N	n	8.8	40	1	60	n	n	+	IM
127	32	M	15	LM	24m	N	N	n	12.8	34	0.9	14	n	n	+	PGLF
128	60	F	12	LM	5m	N	N	n	11	24	1.3	12	n	n	+	AG

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
129	47	M	13	LM	12m	Y	Y	et	12.3	20	0.9	14	n	n	+	PGLF
130	26	M	14	LM	8m	N	N	n	13	34	0.9	34	n	n	-	n
131	45	M	23	UM	7m	N	N	n	12	23	0.8	20	n	n	+	PGLF
132	63	M	13	LM	6m	N	N	n	10	34	1	24	n	n	+	PG
133	57	M	14	LM	7m	N	N	n	12	40	1	30	n	n	+	AG
134	27	F	12	LM	8m	N	N	n	13.2	20	0.7	24	n	n	+	PGLF
135	67	M	11	LM	6m	N	N	et	13	30	1	12	n	n	-	n
136	22	F	11	LM	24m	N	N	n	11	20	0.7	14	n	n	+	PGLF
137	38	F	23	UM	24m	N	N	n	12.8	20	0.9	20	n	n	+	PGIM
138	68	M	12	LM	24m	Y	N	n	8.2	56	3.2	20	n	AG	+	PG
139	60	F	12	LM	3m	N	N	n	12.8	30	1.1	20	n	E	-	n
140	47	M	13	LM	36m	N	N	n	13.4	28	1	30	n	n	+	PG
141	82	M	14	LM	12m	Y	N	n	12	38	1.3	16	n	ER	-	PG
142	62	M	11	LM	6m	Y	Y	et	7.3	50	1.8	50	n	AG	+	PG
143	55	M	11	LM	48m	Y	N	et	9	28	1	48	n	ADU	+	AG
144	70	F	23	UM	6m	N	N	et	12.2	30	1.1	20	n	n	-	n
145	52	M	13	LM	12m	N	N	n	13.2	30	0.9	10	n	n	-	n
146	54	M	11	LM	24m	N	N	n	14	30	0.9	10	n	n	-	n
147	52	M	12	LM	6m	N	N	n	13.9	30	1.2	14	n	n	-	n
148	49	M	15	LM	3m	N	N	n	13.6	40	1.2	26	n	E	-	AG
149	52	M	23	UM	48m	N	N	n	14	32	0.9	10	n	n	-	BGLF
150	33	F	14	LM	3m	N	N	n	12.2	36	0.9	12	n	n	-	n
151	29	M	12	LM	3m	N	N	n	13.6	16	0.9	10	n	n	-	n
152	72	F	13	LM	4m	Y	N	et	6.2	42	1	68	GOO	AGR	-	PDAC
153	33	M	11	LM	24m	N	N	n	13	35	1	12	n	n	+	AGLF
154	56	F	11	LM	6m	N	N	n	13.8	28	0.9	20	FL	n	-	n
155	27	F	13	LM	24m	N	N	n	12	19	0.8	20	n	n	-	n
156	49	M	15	LM	6m	N	N	n	13	36	0.9	22	n	SD	-	n
157	56	F	15	LM	24m	N	N	n	12	26	0.9	20	n	n	-	n
158	32	F	13	LM	6m	N	N	n	12.8	18	0.8	22	FL	n	-	n
159	31	M	21	UM	6m	N	N	n	13	30	0.8	10	FL	n	-	n
160	39	M	13	LM	24m	N	N	n	12.6	18	0.8	22	n	n	-	AGLF

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
161	48	F	12	LM	3m	N	N	n	12	19	0.6	20	FL	n	-	n
162	34	M	11	LM	24m	N	N	n	14	20	0.8	24	n	G	-	PG
163	29	M	21	UM	12m	N	N	n	12.9	20	0.8	10	n	n	-	n
164	43	M	14	LM	12m	N	N	n	13	30	0.7	14	n	n	-	AGLF
165	35	F	15	LM	6m	N	N	et	13	20	0.9	20	FL	n	+	AGLF
166	63	F	15	LM	4m	Y	N	et	6.2	40	0.8	92	n	OGJG	-	PDAC
167	30	M	14	LM	36m	N	N	n	12.2	19	0.8	26	n	ND	-	AGLF
168	40	F	18	UM	6m	Y	N	et	9	20	0.8	90	n	OGJG	-	PDAC
169	55	F	12	LM	36m	N	N	et	12.6	20	0.8	32	FL	n	+	PGLF
170	40	F	12	LM	48m	N	N	et	13	20	0.6	20	n	n	+	PGLF
171	26	M	13	LM	36m	Y	N	et	13.2	19	0.7	40	n	n	+	AGLF
172	46	M	15	LM	3m	Y	N	et	8.2	38	1.4	78	n	OGJG	-	PDAC
173	30	M	19	UM	5m	N	N	n	14	20	0.9	10	n	n	-	n
174	52	F	11	LM	8m	Y	N	et	7	39	1	56	n	OGJG	-	PDAC
175	36	M	11	LM	5m	N	N	n	13.5	28	0.9	10	n	n	-	n
176	40	M	11	LM	7m	N	N	n	12	20	0.9	24	n	n	+	AG
177	24	M	13	LM	36m	N	N	n	14	23	1	14	n	n	+	AGLF
178	36	M	14	LM	3m	N	N	et	12.2	22	0.8	22	n	n	+	FGLF
179	52	F	14	LM	5m	Y	N	et	8.7	34	1	68	n	FGR	-	PDAC
180	52	F	21	UM	12m	N	N	n	13	23	0.8	24	n	n	-	n
181	67	M	12	LM	6m	Y	N	n	7.2	122	4.6	110	n	n	+	PGLF
182	70	M	23	UM	60m	N	N	n	11.8	30	0.8	10	n	n	+	n
183	65	M	15	LM	36m	N	N	et	10	23	1	24	n	ER	+	PGLF
184	50	M	12	LM	5m	N	Y	et	14	23	1	10	n	ER	+	n
185	30	M	21	UM	24m	N	N	et	13.2	23	0.8	12	n	n	+	PG
186	35	M	13	LM	6m	N	N	n	12	30	0.9	14	n	n	+	PG
187	53	M	13	LM	12m	N	N	n	14.2	38	0.9	10	n	n	-	n
188	55	F	15	LM	12m	Y	N	et	9	23	0.8	24	n	n	+	PGLF
189	64	F	21	UM	24m	N	N	n	12.3	24	1.2	40	n	n	+	FGBG
190	60	M	13	LM	4m	Y	N	n	7	40	1.2	60	n	FGR	-	PDAC
191	62	F	12	LM	6m	N	N	n	8.2	50	2.5	130	n	n	+	PGLF
192	36	M	11	LM	12m	N	N	n	14	23	1	34	n	n	-	n

S NO	AGE	SEX	socioeconomic score	socioeconomic status	SYMPTOMS(months)	ALARM SYMPTOMS	SMOKER	ABDOMEN	HEMOGLOBIN(gms/dl)	UREA(mg/dl)	CREATININE(mg/dl)	ESR(mm)	USG	OGD	RUT	BIOPSY
193	39	M	11	LM	24m	N	N	n	13.6	38	1.3	20	n	n	-	AGLF
194	51	M	23	UM	36m	N	N	n	13	24	0.9	20	n	n	+	FGBG
195	40	M	14	LM	6m	Y	N	n	14	24	1	12	n	SD	+	FGAG
196	40	F	15	LM	6m	N	N	n	12.3	20	0.7	10	n	n	-	n
197	65	F	12	LM	24m	N	N	n	10	40	1	20	n	E	-	AG
198	42	F	13	LM	24m	N	N	et	12.8	34	1.2	14	n	n	-	PG
199	38	F	22	UM	24m	N	N	n	11	34	0.7	20	n	n	+	FG
200	65	M	12	LM	36m	N	N	et	12	45	1.2	30	n	n	+	PGLF
201	36	M	12	LM	36m	N	N	n	13	20	0.9	10	n	n	+	PGLF
202	23	F	21	UM	12m	Y	N	n	12.6	23	1	18	n	DUO	+	AGLF
203	67	M	14	LM	12m	N	N	n	13	40	1.2	34	n	n	-	n
204	32	M	19	UM	6m	N	N	n	14	23	1.2	10	n	n	-	n
205	29	M	11	LM	48m	N	N	n	13.7	19	0.8	18	n	n	+	PGLF
206	75	M	14	LM	36m	Y	N	n	10	23	1.3	56	n	E	-	FG
207	37	M	23	UM	48m	N	N	n	12.3	20	0.9	20	n	n	+	AGLF
208	55	M	15	LM	6m	Y	Y	n	10	34	1.4	24	n	E	-	FG
209	38	M	14	LM	5m	N	N	n	14	23	1.4	10	n	n	-	n
210	28	M	11	LM	6m	N	N	n	13.8	23	0.6	10	n	n	-	PG
211	35	M	21	UM	12m	Y	N	n	12	24	1.3	24	n	SD	+	PGLF
212	40	F	12	LM	3m	N	N	n	11.8	20	1.2	34	n	n	+	PG
213	32	F	13	LM	6m	N	N	n	12	20	0.9	18	n	n	-	n
214	58	M	15	LM	24m	N	N	n	11.6	40	1.4	20	n	n	+	PGLF
215	42	F	22	UM	36m	Y	N	n	6.2	34	1	60	n	HG	-	PDAC
216	58	M	12	LM	8m	N	N	n	11.2	45	1	36	n	n	-	n
217	56	F	12	LM	9m	N	N	n	12	36	1	40	n	ER	-	PG
218	55	M	11	LM	12m	N	N	n	13	40	1	28	n	E	-	PG
219	27	M	15	LM	24m	N	N	et	13.9	24	0.7	10	n	n	-	n
220	43	M	20	UM	6m	N	N	et	14	26	1.2	24	n	n	-	n
221	48	M	13	LM	12m	Y	N	et	10	24	1.2	30	n	ADU	+	AGLF
222	64	F	12	LM	4m	N	N	et	12.2	40	1.4	28	n	n	+	AG
223	43	M	18	UM	6m	N	N	et	14	26	1.3	40	n	n	-	PG
224	23	F	20	UM	5m	N	N	n	12	24	0.6	10	n	n	-	n

KEY TO MASTER CHART

+ Positive

- Negative

ADU - Acute Duodenal Ulcer

AG - Antral Gastritis

AGR - Antral Growth

BG - Gastritis of Body

CDU - Chronic Duodenal Ulcer

DB - Deformed Bulb

DUO - Duodenal Ulcer with Obstruction

E - Esophagitis

ER - Erosive Gastritis

ESR- Erythrocyte Sedimentation Rate

ET – Epigastric Tenderness

F - Female

FG - Fundal Gastritis

FGR - Fundal Growth

FL - Fatty Liver

GOO - Gastric Outlet Obstruction

HG - Hypertrophic Gastritis

IM - Intestinal Metaplasia

L – Lower Socioeconomic Class

LF - Lymphoid Follicles

LM – Lower Middle Socioeconomic Class

M - Male

m – Months

n – Normal

N – No

ND - Nodular Duodenum

OGD - Endoscopy

OGJG - Oesophagogastric Junction Growth

PDAC - Poorly Differentiated Adenocarcinoma

PG - Pan Gastritis

RUT - Rapid Urease Test

SD - Scarred Duodenum

Y – Yes

UL – Upper Lower Socioeconomic Class

UM – Upper Middle Socioeconomic Class

USG - Ultrasonogram